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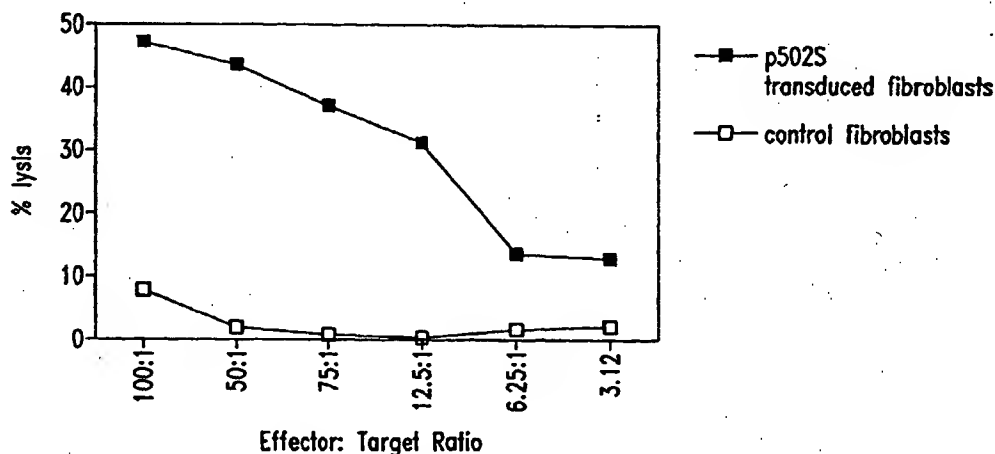
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(54) Title: COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF PROSTATE CANCER



(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate tumor proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate tumor protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate tumor protein, or mRNA encoding such a protein, in a sample are also provided.

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## COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF PROSTATE CANCER

### TECHNICAL FIELD

The present invention relates generally to therapy and diagnosis of cancer, such as prostate cancer. The invention is more specifically related to polypeptides comprising at least a portion of a prostate tumor protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers.

### BACKGROUND OF THE INVENTION

Prostate cancer is the most common form of cancer among males, with an estimated incidence of 30% in men over the age of 50. Overwhelming clinical evidence shows that human prostate cancer has the propensity to metastasize to bone, and the disease appears to progress inevitably from androgen dependent to androgen refractory status, leading to increased patient mortality. This prevalent disease is currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate cancer remains difficult to treat. Commonly, treatment is based on surgery and/or radiation therapy, but these methods are ineffective in a significant percentage of cases. Two previously identified prostate specific proteins - prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic potential. For example, PSA levels do not always correlate well with the presence of prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating

such cancers. The present invention fulfills these needs and further provides other related advantages.

#### SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the diagnosis and therapy of cancer, such as prostate cancer. In one aspect, the present invention provides polypeptides comprising at least a portion of a prostate tumor protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises at least an immunogenic portion of a prostate tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472; (b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and (c) complements of any of the sequence of (a) or (b). In certain specific embodiments, such a polypeptide comprises at least a portion, or variant thereof, of a tumor protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380 and 383.

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a prostate tumor protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and a non-specific immune response enhancer.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a prostate tumor protein; and (b) a physiologically acceptable carrier.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a non-specific immune response enhancer.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a non-specific immune response enhancer.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate tumor protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a prostate tumor protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a prostate tumor protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be prostate cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount

detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

#### BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate tumor polypeptide P502S, as compared to control fibroblasts. The percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate tumor polypeptide P502S. In each case, the number of  $\gamma$ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/*neu*.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2Kb cells expressing the representative prostate tumor polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

Figures 6A and 6B are graphs illustrating the specificity of a CD8<sup>+</sup> cell line (3A-1) for a representative prostate tumor antigen (P501S). Figure 6A shows the results of a <sup>51</sup>Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target ratios as indicated.

SEQ ID NO: 1 is the determined cDNA sequence for F1-13

SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12

SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16

SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1

SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9

SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4

SEQ ID NO: 8 is the determined 3' cDNA sequence for J1-17

SEQ ID NO: 9 is the determined 5' cDNA sequence for J1-17

SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12

SEQ ID NO: 11 is the determined 5' cDNA sequence for L1-12

SEQ ID NO: 12 is the determined 3' cDNA sequence for N1-1862

SEQ ID NO: 13 is the determined 5' cDNA sequence for N1-1862

SEQ ID NO: 14 is the determined 3' cDNA sequence for J1-13

SEQ ID NO: 15 is the determined 5' cDNA sequence for J1-13

SEQ ID NO: 16 is the determined 3' cDNA sequence for J1-19

SEQ ID NO: 17 is the determined 5' cDNA sequence for J1-19

SEQ ID NO: 18 is the determined 3' cDNA sequence for J1-25

SEQ ID NO: 19 is the determined 5' cDNA sequence for J1-25

SEQ ID NO: 20 is the determined 5' cDNA sequence for J1-24



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SEQ ID NO: 31 is the determined 3' cDNA sequence for J1-16  
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SEQ ID NO: 44 is the determined cDNA sequence for P18  
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SEQ ID NO: 47 is the determined cDNA sequence for P30  
SEQ ID NO: 48 is the determined cDNA sequence for P34  
SEQ ID NO: 49 is the determined cDNA sequence for P36  
SEQ ID NO: 50 is the determined cDNA sequence for P38

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SEQ ID NO: 236 is the determined cDNA sequence for PTPN35  
SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36  
SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38  
SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39  
SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40  
SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41  
SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42  
SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45  
SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46  
SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51  
SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56  
SEQ ID NO: 247 is the determined cDNA sequence for PTPN64  
SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65  
SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67  
SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76  
SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84  
SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85  
SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86  
SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87  
SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88  
SEQ ID NO: 256 is the determined cDNA sequence for JP1F1  
SEQ ID NO: 257 is the determined cDNA sequence for JP1F2  
SEQ ID NO: 258 is the determined cDNA sequence for JP1C2



SEQ ID NO: 259 is the determined cDNA sequence for JP1B1  
SEQ ID NO: 260 is the determined cDNA sequence for JP1B2  
SEQ ID NO: 261 is the determined cDNA sequence for JP1D3  
SEQ ID NO: 262 is the determined cDNA sequence for JP1A4  
SEQ ID NO: 263 is the determined cDNA sequence for JP1F5  
SEQ ID NO: 264 is the determined cDNA sequence for JP1E6  
SEQ ID NO: 265 is the determined cDNA sequence for JP1D6  
SEQ ID NO: 266 is the determined cDNA sequence for JP1B5  
SEQ ID NO: 267 is the determined cDNA sequence for JP1A6  
SEQ ID NO: 268 is the determined cDNA sequence for JP1E8  
SEQ ID NO: 269 is the determined cDNA sequence for JP1D7  
SEQ ID NO: 270 is the determined cDNA sequence for JP1D9  
SEQ ID NO: 271 is the determined cDNA sequence for JP1C10  
SEQ ID NO: 272 is the determined cDNA sequence for JP1A9  
SEQ ID NO: 273 is the determined cDNA sequence for JP1F12  
SEQ ID NO: 274 is the determined cDNA sequence for JP1E12  
SEQ ID NO: 275 is the determined cDNA sequence for JP1D11  
SEQ ID NO: 276 is the determined cDNA sequence for JP1C11  
SEQ ID NO: 277 is the determined cDNA sequence for JP1C12  
SEQ ID NO: 278 is the determined cDNA sequence for JP1B12  
SEQ ID NO: 279 is the determined cDNA sequence for JP1A12  
SEQ ID NO: 280 is the determined cDNA sequence for JP8G2  
SEQ ID NO: 281 is the determined cDNA sequence for JP8H1  
SEQ ID NO: 282 is the determined cDNA sequence for JP8H2  
SEQ ID NO: 283 is the determined cDNA sequence for JP8A3  
SEQ ID NO: 284 is the determined cDNA sequence for JP8A4  
SEQ ID NO: 285 is the determined cDNA sequence for JP8C3  
SEQ ID NO: 286 is the determined cDNA sequence for JP8G4  
SEQ ID NO: 287 is the determined cDNA sequence for JP8B6  
SEQ ID NO: 288 is the determined cDNA sequence for JP8D6

SEQ ID NO: 289 is the determined cDNA sequence for JP8F5  
SEQ ID NO: 290 is the determined cDNA sequence for JP8A8  
SEQ ID NO: 291 is the determined cDNA sequence for JP8C7  
SEQ ID NO: 292 is the determined cDNA sequence for JP8D7  
SEQ ID NO: 293 is the determined cDNA sequence for P8D8  
SEQ ID NO: 294 is the determined cDNA sequence for JP8E7  
SEQ ID NO: 295 is the determined cDNA sequence for JP8F8  
SEQ ID NO: 296 is the determined cDNA sequence for JP8G8  
SEQ ID NO: 297 is the determined cDNA sequence for JP8B10  
SEQ ID NO: 298 is the determined cDNA sequence for JP8C10  
SEQ ID NO: 299 is the determined cDNA sequence for JP8E9  
SEQ ID NO: 300 is the determined cDNA sequence for JP8E10  
SEQ ID NO: 301 is the determined cDNA sequence for JP8F9  
SEQ ID NO: 302 is the determined cDNA sequence for JP8H9  
SEQ ID NO: 303 is the determined cDNA sequence for JP8C12  
SEQ ID NO: 304 is the determined cDNA sequence for JP8E11  
SEQ ID NO: 305 is the determined cDNA sequence for JP8E12  
SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12  
SEQ ID NO: 307 is the determined cDNA sequence for P711P  
SEQ ID NO: 308 is the determined cDNA sequence for P712P  
SEQ ID NO: 309 is the determined cDNA sequence for CLONE23  
SEQ ID NO: 310 is the determined cDNA sequence for P774P  
SEQ ID NO: 311 is the determined cDNA sequence for P775P  
SEQ ID NO: 312 is the determined cDNA sequence for P715P  
SEQ ID NO: 313 is the determined cDNA sequence for P710P  
SEQ ID NO: 314 is the determined cDNA sequence for P767P  
SEQ ID NO: 315 is the determined cDNA sequence for P768P  
SEQ ID NO: 316-325 are the determined cDNA sequences of previously isolated genes  
SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5  
SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5

SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26

SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26

SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23

SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23

SEQ ID NO: 332 is the determined full length cDNA sequence for P509S

SEQ ID NO: 333 is the determined extended cDNA sequence for P707P (also referred to as 11-C9)

SEQ ID NO: 334 is the determined cDNA sequence for P714P

SEQ ID NO: 335 is the determined cDNA sequence for P705P (also referred to as 9-F3)

SEQ ID NO: 336 is the predicted amino acid sequence for P705P

SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10

SEQ ID NO: 338 is the amino acid sequence of the peptide p5

SEQ ID NO: 339 is the predicted amino acid sequence of P509S

SEQ ID NO: 340 is the determined cDNA sequence for P778P

SEQ ID NO: 341 is the determined cDNA sequence for P786P

SEQ ID NO: 342 is the determined cDNA sequence for P789P

SEQ ID NO: 343 is the determined cDNA sequence for a clone showing homology to Homo sapiens MM46 mRNA

SEQ ID NO: 344 is the determined cDNA sequence for a clone showing homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA

SEQ ID NO: 345 is the determined cDNA sequence for a clone showing homology to Homo sapiens mRNA for E-cadherin

SEQ ID NO: 346 is the determined cDNA sequence for a clone showing homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase (SHMT)

SEQ ID NO: 347 is the determined cDNA sequence for a clone showing homology to Homo sapiens natural resistance-associated macrophage protein2 (NRAMP2)

SEQ ID NO: 348 is the determined cDNA sequence for a clone showing homology to Homo sapiens phosphoglucomutase-related protein (PGMRP)

SEQ ID NO: 349 is the determined cDNA sequence for a clone showing homology to Human mRNA for proteosome subunit p40

SEQ ID NO: 350 is the determined cDNA sequence for P777P

SEQ ID NO: 351 is the determined cDNA sequence for P779P

SEQ ID NO: 352 is the determined cDNA sequence for P790P

SEQ ID NO: 353 is the determined cDNA sequence for P784P

SEQ ID NO: 354 is the determined cDNA sequence for P776P

SEQ ID NO: 355 is the determined cDNA sequence for P780P

SEQ ID NO: 356 is the determined cDNA sequence for P544S

SEQ ID NO: 357 is the determined cDNA sequence for P745S

SEQ ID NO: 358 is the determined cDNA sequence for P782P

SEQ ID NO: 359 is the determined cDNA sequence for P783P

SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984

SEQ ID NO: 361 is the determined cDNA sequence for P787P

SEQ ID NO: 362 is the determined cDNA sequence for P788P

SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994

SEQ ID NO: 364 is the determined cDNA sequence for P781P

SEQ ID NO: 365 is the determined cDNA sequence for P785P

SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.

SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 366.

SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372.

SEQ ID NO: 378 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 373.

SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 374.

SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 375.

SEQ ID NO: 381 is the determined cDNA sequence for B716P.  
SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.  
SEQ ID NO: 383 is the predicted amino acid sequence for P711P.  
SEQ ID NO: 384 is the cDNA sequence for P1000C.  
SEQ ID NO: 385 is the cDNA sequence for CGI-82.  
SEQ ID NO:386 is the cDNA sequence for 23320.  
SEQ ID NO:387 is the cDNA sequence for CGI-69.  
SEQ ID NO:388 is the cDNA sequence for L-iditol-2-dehydrogenase.  
SEQ ID NO:389 is the cDNA sequence for 23379.  
SEQ ID NO:390 is the cDNA sequence for 23381.  
SEQ ID NO:391 is the cDNA sequence for KIAA0122.  
SEQ ID NO:392 is the cDNA sequence for 23399.  
SEQ ID NO:393 is the cDNA sequence for a previously identified gene.  
SEQ ID NO:394 is the cDNA sequence for HCLBP.  
SEQ ID NO:395 is the cDNA sequence for transglutaminase.  
SEQ ID NO:396 is the cDNA sequence for a previously identified gene.  
SEQ ID NO:397 is the cDNA sequence for PAP.  
SEQ ID NO:398 is the cDNA sequence for Ets transcription factor PDEF.  
SEQ ID NO:399 is the cDNA sequence for hTGR.  
SEQ ID NO:400 is the cDNA sequence for KIAA0295.  
SEQ ID NO:401 is the cDNA sequence for 22545.  
SEQ ID NO:402 is the cDNA sequence for 22547.  
SEQ ID NO:403 is the cDNA sequence for 22548.  
SEQ ID NO:404 is the cDNA sequence for 22550.  
SEQ ID NO:405 is the cDNA sequence for 22551.  
SEQ ID NO:406 is the cDNA sequence for 22552.  
SEQ ID NO:407 is the cDNA sequence for 22553.  
SEQ ID NO:408 is the cDNA sequence for 22558.  
SEQ ID NO:409 is the cDNA sequence for 22562.  
SEQ ID NO:410 is the cDNA sequence for 22565.

SEQ ID NO:411 is the cDNA sequence for 22567.  
SEQ ID NO:412 is the cDNA sequence for 22568.  
SEQ ID NO:413 is the cDNA sequence for 22570.  
SEQ ID NO:414 is the cDNA sequence for 22571.  
SEQ ID NO:415 is the cDNA sequence for 22572.  
SEQ ID NO:416 is the cDNA sequence for 22573.  
SEQ ID NO:417 is the cDNA sequence for 22573.  
SEQ ID NO:418 is the cDNA sequence for 22575.  
SEQ ID NO:419 is the cDNA sequence for 22580.  
SEQ ID NO:420 is the cDNA sequence for 22581.  
SEQ ID NO:421 is the cDNA sequence for 22582.  
SEQ ID NO:422 is the cDNA sequence for 22583.  
SEQ ID NO:423 is the cDNA sequence for 22584.  
SEQ ID NO:424 is the cDNA sequence for 22585.  
SEQ ID NO:425 is the cDNA sequence for 22586.  
SEQ ID NO:426 is the cDNA sequence for 22587.  
SEQ ID NO:427 is the cDNA sequence for 22588.  
SEQ ID NO:428 is the cDNA sequence for 22589.  
SEQ ID NO:429 is the cDNA sequence for 22590.  
SEQ ID NO:430 is the cDNA sequence for 22591.  
SEQ ID NO:431 is the cDNA sequence for 22592.  
SEQ ID NO:432 is the cDNA sequence for 22593.  
SEQ ID NO:433 is the cDNA sequence for 22594.  
SEQ ID NO:434 is the cDNA sequence for 22595.  
SEQ ID NO:435 is the cDNA sequence for 22596.  
SEQ ID NO:436 is the cDNA sequence for 22847.  
SEQ ID NO:437 is the cDNA sequence for 22848.  
SEQ ID NO:438 is the cDNA sequence for 22849.  
SEQ ID NO:439 is the cDNA sequence for 22851.  
SEQ ID NO:440 is the cDNA sequence for 22852.

SEQ ID NO:441 is the cDNA sequence for 22853.  
SEQ ID NO:442 is the cDNA sequence for 22854.  
SEQ ID NO:443 is the cDNA sequence for 22855.  
SEQ ID NO:444 is the cDNA sequence for 22856.  
SEQ ID NO:445 is the cDNA sequence for 22857.  
SEQ ID NO:446 is the cDNA sequence for 23601.  
SEQ ID NO:447 is the cDNA sequence for 23602.  
SEQ ID NO:448 is the cDNA sequence for 23605.  
SEQ ID NO:449 is the cDNA sequence for 23606.  
SEQ ID NO:450 is the cDNA sequence for 23612.  
SEQ ID NO:451 is the cDNA sequence for 23614.  
SEQ ID NO:452 is the cDNA sequence for 23618.  
SEQ ID NO:453 is the cDNA sequence for 23622.  
SEQ ID NO:454 is the cDNA sequence for folate hydrolase.  
SEQ ID NO:455 is the cDNA sequence for LIM protein.  
SEQ ID NO:456 is the cDNA sequence for a known gene.  
SEQ ID NO:457 is the cDNA sequence for a known gene.  
SEQ ID NO:458 is the cDNA sequence for a previously identified gene.  
SEQ ID NO:459 is the cDNA sequence for 23045.  
SEQ ID NO:460 is the cDNA sequence for 23032.  
SEQ ID NO:461 is the cDNA sequence for 23054.  
SEQ ID NOs:462-467 are cDNA sequences for known genes.  
SEQ ID NOs:468-471 are cDNA sequences for P710P.  
SEQ ID NO:472 is a cDNA sequence for P1001C.  
SEQ ID NO:473 is the amino acid sequence for PSMA.  
SEQ ID NO:474 is the amino acid sequence for PAP.  
SEQ ID NO:475 is the amino acid sequence for PSA.  
SEQ ID NO:476 is the amino acid sequence for a fusion protein containing PSA, P703P and P501S.

## DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer. The compositions described herein may include prostate tumor polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (*e.g.*, T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a prostate tumor protein or a variant thereof. A "prostate tumor protein" is a protein that is expressed in prostate tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a normal tissue, as determined using a representative assay provided herein. Certain prostate tumor proteins are tumor proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with prostate cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery of human prostate tumor proteins. Sequences of polynucleotides encoding certain tumor proteins, or portions thereof, are provided in SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472. Sequences of polypeptides comprising at least a portion of a tumor protein are provided in SEQ ID NOs:112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380 and 383.



## PROSTATE TUMOR PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a prostate tumor protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a prostate tumor protein. More preferably, a polynucleotide encodes an immunogenic portion of a prostate tumor protein. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a prostate tumor protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native tumor protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native prostate tumor protein or a portion thereof.

Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions,

usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are

capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native prostate tumor protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least five fold greater in a prostate tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as prostate tumor cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

An amplified portion may be used to isolate a full length gene from a suitable library (e.g., a prostate tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with  $^{32}\text{P}$ ) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (*see* Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (*e.g.*, NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence.

Certain nucleic acid sequences of cDNA molecules encoding at least a portion of a prostate tumor protein are provided in SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472. Isolation of these polynucleotides is described below. Each of these prostate tumor proteins was overexpressed in prostate tumor tissue.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may

also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (see Adelman et al., *DNA* 2:183, 1983). Alternatively, RNA molecules may be generated by *in vitro* or *in vivo* transcription of DNA sequences encoding a prostate tumor protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated *in vivo* (e.g., by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a prostate tumor polypeptide, and administering the transfected cells to the patient).

A portion of a sequence complementary to a coding sequence (*i.e.*, an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a tumor protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (see Gee et al., *In Huber and Carr, Molecular and Immunologic Approaches*, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (e.g., promoter, enhancer or transcription initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl-, methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In general, a vector will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (*e.g.*, avian pox virus). Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane vesicle). The preparation and use of such systems is well known in the art.

#### PROSTATE TUMOR POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a prostate tumor protein or a variant thereof, as described herein. As noted above, a "prostate tumor protein" is a protein that is expressed by prostate tumor cells. Proteins that are prostate tumor proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with prostate cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a prostate tumor protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera



and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native prostate tumor protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, <sup>125</sup>I-labeled Protein A.

As noted above, a composition may comprise a variant of a native prostate tumor protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native prostate tumor protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein. Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most

preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydrophatic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydrophatic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression

vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast and higher eukaryotic cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be

targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

In certain embodiments, the present invention provides fusion proteins comprising a polypeptide disclosed herein together with at least one of the following known prostate antigens: prostate specific antigen (PSA); prostatic acid phosphatase (PAP); and prostate specific membrane antigen (PSMA). The protein sequences for PSMA, PAP and PSA are provided in SEQ ID NO: 473-475, respectively. In certain embodiments, the fusion proteins of the present invention comprise PSA, PAP and/or PSMA in combination with one or more of the following the inventive antigens: P501S (amino acid sequence provided in SEQ ID NO: 113); P703P (amino acid sequences provided in SEQ ID NO: 327, 329, 331); P704P (cDNA sequence provided in SEQ ID NO: 67); P712P (cDNA sequence provided in SEQ ID NO: 308); P775P (cDNA sequence provided in SEQ ID NO: 311); P776P (cDNA sequence provided in SEQ ID NO: 354); P790P (cDNA sequence provided in SEQ ID NO: 352). The amino acid sequence of a fusion protein of PSA, P703P and P501S is provided in SEQ ID NO: 476. In preferred embodiments, the inventive fusion proteins comprise one of the following combinations of antigens: PSA and P703P; PSA and P501S; PAP and P703P; PAP and P501S; PSMA and P703P; PSMA and P501S; PSA, PAP and P703P; PSA, PAP and P501S; PSA, PAP, PSMA and P703P, PSA, PAP, PSMA and P501S. One of skill in the art will appreciate that the order of polypeptides within a fusion protein can be altered without substantially changing the therapeutic, prophylactic or diagnostic properties of the fusion protein.

The fusion proteins described above are more immunogenic and will be effective in a greater number of prostate cancer patients than any of the individual components alone. The use of multiple antigens in the form of a fusion protein also lessens the likelihood of immunologic escape.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide

components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (*see, for example, Stoute et al. New Engl. J. Med.*, 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology* 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-

terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector that is not a part of the natural environment.

#### BINDING AGENTS

The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a prostate tumor protein. As used herein, an antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a prostate tumor protein if it reacts at a detectable level (within, for example, an ELISA) with a prostate tumor protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about  $10^3$  L/mol. The binding constant may be determined using methods well known in the art.

Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a prostate tumor protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal

indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (e.g., blood, sera, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. *See, e.g.,* Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.



Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988) and digested

by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include  $^{90}\text{Y}$ ,  $^{123}\text{I}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{211}\text{At}$ , and  $^{212}\text{Bi}$ . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

#### T CELLS

Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a prostate tumor protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the CEPRATE™ system, available from CellPro Inc., Bothell WA (*see also* U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a prostate tumor polypeptide, polynucleotide encoding a prostate tumor polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a prostate tumor polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a prostate tumor polypeptide if the T cells kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively,

detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a prostate tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-γ) is indicative of T cell activation (see Coligan et al., Current Protocols in Immunology, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a prostate tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4<sup>+</sup> and/or CD8<sup>+</sup>. Prostate tumor protein-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4<sup>+</sup> or CD8<sup>+</sup> T cells that proliferate in response to a prostate tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a prostate tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a prostate tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of a prostate tumor protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

#### PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions

or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and a non-specific immune response enhancer. A non-specific immune response enhancer may be any substance that enhances an immune response to an exogenous antigen. Examples of non-specific immune response enhancers include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (*e.g.*, vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner

et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA or glutathione, adjuvants (e.g., aluminum hydroxide) and/or preservatives. Alternatively, compositions of the present invention may be

formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of non-specific immune response enhancers may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (*e.g.*, IFN- $\gamma$ , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (*e.g.*, IL-4, IL-5, IL-6, IL-10 and TNF- $\beta$ ) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt.



MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT; see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release formulation (*i.e.*, a formulation such as a capsule or sponge that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained within a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific

immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*) and based on the lack of differentiation markers of B cells (CD19 and CD20), T cells (CD3), monocytes (CD14) and natural killer cells (CD56), as determined using standard assays. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF $\alpha$  to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into

dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF $\alpha$ , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc $\gamma$  receptor, mannose receptor and DEC-205 marker. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80 and CD86).

APCs may generally be transfected with a polynucleotide encoding a prostate tumor protein (or portion or other variant thereof) such that the prostate tumor polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the prostate tumor polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be

pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

#### CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as prostate cancer. Within such methods, pharmaceutical compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8<sup>+</sup> cytotoxic T lymphocytes and CD4<sup>+</sup> T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The

polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see, for example, Cheever et al., Immunological Reviews 157:177, 1997*).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g., intracutaneous,*

intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 100  $\mu$ g to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a prostate tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

#### METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or more prostate tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, urine and/or tumor biopsies) obtained from

the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. *See, e.g.,* Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length prostate tumor proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10  $\mu$ g, and preferably about 100 ng to about 1  $\mu$ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.,* Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized



on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed

and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (i.e., sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (i.e., the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1  $\mu$ g, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use prostate tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such prostate tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a prostate tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient is incubated with a prostate tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with prostate tumor polypeptide (*e.g.*, 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of prostate tumor polypeptide to serve as a control. For CD4<sup>+</sup> T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8<sup>+</sup> T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a prostate tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a prostate tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the prostate tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a prostate tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%,

preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a prostate tumor protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375 and 381. Techniques for both PCR based assays and hybridization assays are well known in the art (*see, for example, Mullis et al., Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter

performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple prostate tumor protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

#### DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a prostate tumor protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a prostate tumor protein in a biological sample. Such kits generally comprise

at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a prostate tumor protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a prostate tumor protein.

The following Examples are offered by way of illustration and not by way of limitation.

## EXAMPLES

### EXAMPLE 1

#### ISOLATION AND CHARACTERIZATION OF PROSTATE TUMOR POLYPEPTIDES

This Example describes the isolation of certain prostate tumor polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from prostate tumor poly A<sup>+</sup> RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol. Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A<sup>+</sup> RNA was then purified using a Qiagen oligotex spin column mRNA purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with Chroma Spin-1000 columns (Clontech, Palo Alto, CA), the cDNA was ligated into the EcoRI/NotI site of pCDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was prepared from a pool of six tissue specimens (Clontech). The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The prostate tumor library contained  $1.64 \times 10^7$  independent colonies, with 70% of clones having an insert and the average insert size being 1745 base pairs. The normal pancreas cDNA library contained  $3.3 \times 10^6$  independent colonies, with 69% of clones



having inserts and the average insert size being 1120 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

cDNA library subtraction was performed using the above prostate tumor and normal pancreas cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, NotI, and SfuI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 100 µl of H<sub>2</sub>O, heat-denatured and mixed with 100 µl (100 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 µl H<sub>2</sub>O to form the driver DNA.

To form the tracer DNA, 10 µg prostate tumor cDNA library was digested with BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 µl H<sub>2</sub>O. Tracer DNA was mixed with 15 µl driver DNA and 20 µl of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 µl H<sub>2</sub>O, mixed with 8 µl driver DNA and 20 µl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK<sup>+</sup> (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax E.

*coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively, with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12. This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1  $\mu$ g each of human glandular kallikrein, PSA and mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the

driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively). Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to *R. norvegicus* mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA library with spike, four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show some homology to known human sequences. No significant homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding predicted amino acid sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein, mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807, 1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193,

respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were over-expressed in most prostate tumors and prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the identification of six additional clones referred to as 1G-4761, 1G-4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 199, respectively, and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA+ RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297, 1D-4309, 1D-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339.

## EXAMPLE 2

### DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE TUMOR POLYPEPTIDES

Using gene specific primers, mRNA expression levels for the representative prostate tumor polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 1-2  $\mu$ g of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR,  $\beta$ -actin was used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed using  $\beta$ -actin specific primers. A dilution was then chosen that enabled the linear range amplification of the  $\beta$ -actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the  $\beta$ -actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in four different types of tumor tissue (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found to be expressed at high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH prostates, and normal colon, kidney, liver, lung, pancreas, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney, but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-



expressed in prostate tumor and normal prostate, expressed at lower levels in normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatzis *et al.* (*Proc. Natl. Acad. Sci. USA* 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was found to show some homology to the previously isolated Human mRNA for JM27 protein. No significant homologies were found to the sequence of P1000C.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive

cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver, brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

### EXAMPLE 3

#### ISOLATION AND CHARACTERIZATION OF PROSTATE TUMOR POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA subtraction library, containing cDNA from normal prostate subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' *E. coli* (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to

previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

Further studies using the PCR-based methodology described above resulted in the isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145, 147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-170) were found to have some degree of homology to known genes. Larger cDNA clones containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA sequence for an extended spliced form of P703 is provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary (n=2), skeletal muscle, skin, stomach, small intestine and brain), and activated and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed comparable expression. P20, a portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of 2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor

compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal prostate and prostate tumor, compared to six of twelve other normal tissues tested. Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However, substantial expression of P29 was observed in normal colon and normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

mRNA expression levels for these clones were determined using the micro-array technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable. Increased expression of 8-F11 was seen in prostate tumor

and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.

An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both microarray technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those in the public databases revealed 99% identity to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

PCR and hybridization-based methodologies were employed to obtain longer cDNA sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX\_23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of the putative signal sequence. Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are provided in SEQ ID NO: 307-311, 313 and 315, respectively.

The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold over-expression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal prostate tissues (n=4), but background to low expression levels in all normal tissues. Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no significant homologies to P714P were found.

Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted

amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

#### EXAMPLE 4

##### SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

#### EXAMPLE 5

##### FURTHER ISOLATION AND CHARACTERIZATION OF PROSTATE TUMOR POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were

separately digested with five restriction enzymes that recognize six-nucleotide restriction sites (MluI, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JTPN23 (SEQ ID NO: 231; similarity to pig



valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat *norvegicus* cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to *G. gallus* dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most recent release of GenBank revealed no significant homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most prostate tumors and BPH tissues by a factor of three or greater, with elevated expression seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low expression in all other normal tissues tested.

Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349, 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be

expressed in small intestine. Of the 26 clones, 10 (SEQ ID NO: 340-349) were found to show some homology to previously identified sequences. No significant homologies were found to the clones of SEQ ID NO: 350-365.

## EXAMPLE 6

### PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

Mice expressing the transgene for human HLA A2.1 (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID NO: 8), as described by Theobald et al., *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995 with the following modifications. Mice were immunized with 100 $\mu$ g of P2S#12 and 120 $\mu$ g of an I-A<sup>b</sup> binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at  $6 \times 10^6$  cells/ml in complete media (RPMI-1640; Gibco BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL),  $2 \times 10^{-5}$  M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml  $\beta$ 2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7 $\mu$ g/ml dextran sulfate and 25 $\mu$ g/ml LPS for 3 days). Six days later, cells ( $5 \times 10^5$ /ml) were restimulated with  $2.5 \times 10^6$ /ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, *Science* 258:815-818, 1992) and  $3 \times 10^6$ /ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells ( $1 \times 10^4$  cells/ well) as stimulators and A2 transgenic spleen cells

as feeders (  $5 \times 10^5$  cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2.1 expressing) transduced with P502S than against control fibroblasts. An example is presented in Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2.1 molecule.

6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, *et al*, *J. Immunol.*, 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200  $\mu\text{g/ml}$  were added to cultures of D150M58 CTL in order to bind HLA-A2 on the CTL. After thirty minutes, CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

Mice expressing the transgene for human HLA A2.1 were immunized as described by Theobald et al. (*Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5 $\mu\text{g}$  of P1S #10 and 120 $\mu\text{g}$

of an I-A<sup>b</sup> binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared using a nylon mesh. Cells were then resuspended at  $6 \times 10^6$  cells/ml in complete media (as described above) and cultured in the presence of irradiated (3000 rads) P1S#10-pulsed ( $2\mu\text{g/ml}$  P1S#10 and  $10\text{mg/ml}$   $\beta 2$ -microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of  $7\mu\text{g/ml}$  dextran sulfate and  $25\mu\text{g/ml}$  LPS for 3 days). Six days later cells ( $5 \times 10^5/\text{ml}$ ) were restimulated with  $2.5 \times 10^6/\text{ml}$  peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and  $3 \times 10^6/\text{ml}$  A2 transgenic spleen feeder cells. Cells were cultured in the presence of  $20 \text{ U/ml}$  IL-2. Cells were restimulated on a weekly basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells ( $1 \times 10^4$  cells/ well) as stimulators and A2 transgenic spleen cells as feeders ( $5 \times 10^5$  cells/ well) grown in the presence of  $30\text{U/ml}$  IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were isolated and maintained in culture. As shown in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

#### EXAMPLE 7

#### ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE TUMOR POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate tumor polypeptide to recognize human tumor.

Human CD8<sup>+</sup> T cells were primed *in vitro* to the P2S-12 peptide (SEQ ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells according to the protocol of Van Tsai et al. (*Critical Reviews in Immunology* 18:65-75, 1998). The resulting CD8<sup>+</sup> T cell microcultures were tested for their ability to recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which were transduced to express the P502S gene in a  $\gamma$ -interferon ELISPOT assay (see Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). Briefly, titrating numbers of T cells were assayed in duplicate on 10<sup>4</sup> fibroblasts in the presence of 3  $\mu$ g/ml human  $\beta_2$ -microglobulin and 1  $\mu$ g/ml P2S-12 peptide or control E75 peptide. In addition, T cells were simultaneously assayed on autologous fibroblasts transduced with the P502S gene or as a control, fibroblasts transduced with HER-2/*neu*. Prior to the assay, the fibroblasts were treated with 10 ng/ml  $\gamma$ -interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a  $\gamma$ -interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of  $\gamma$ -interferon spots with increasing numbers of T cells on fibroblasts pulsed with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of  $\gamma$ -interferon spots with increasing numbers of T cells on fibroblasts transduced to express the P502S gene but not the HER-2/*neu* gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

## EXAMPLE 8

PRIMING OF CTL *IN VIVO* USING NAKED DNA IMMUNIZATION WITH A PROSTATE ANTIGEN

The prostate tumor antigen L1-12, as described above, is also referred to as P501S. HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with 100 µg VR10132-P501S either intramuscularly or intradermally. The mice were immunized three times, with a two week interval between immunizations. Two weeks after the last immunization, immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL activity was assessed against P501S transduced targets. Two out of 8 mice developed strong anti-P501S CTL responses. These results demonstrate that P501S contains at least one naturally processed A2-restricted CTL epitope.

## EXAMPLE 9

GENERATION OF HUMAN CTL *IN VITRO* USING WHOLE GENE PRIMING AND STIMULATION TECHNIQUES WITH PROSTATE TUMOR ANTIGEN

Using *in vitro* whole-gene priming with P501S-retrovirally transduced autologous fibroblasts (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996), human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon-γ ELISPOT analysis as described above. Using a panel of HLA-mismatched fibroblast lines transduced with P501S, these CTL lines were shown to be restricted HLA-A2 class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a multiplicity of infection (M.O.I) of five, and matured.

overnight by the addition of 3 µg/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8<sup>+</sup> T cells were isolated using a magnetic bead system, and priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S. Following four stimulation cycles, CD8<sup>+</sup> T cell lines were identified that specifically produced interferon-γ when stimulated with P501S-transduced autologous fibroblasts. The P501S-specific activity could be sustained by the continued stimulation of the cultures with P501S-transduced fibroblasts in the presence of IL-15. A panel of HLA-mismatched fibroblast lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon-γ in an ELISPOT assay, the P501S specific response was shown to be restricted by HLA-A2. These results demonstrate that a CD8<sup>+</sup> CTL response to P501S can be elicited.

#### EXAMPLE 10

##### IDENTIFICATION OF A NATURALLY PROCESSED CTL EPITOPE CONTAINED WITHIN A PROSTATE TUMOR ANTIGEN

The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific CD8<sup>+</sup> T cells can be primed following repeated *in vitro* stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2 transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of P703P transduced target cells expressing either HLA-A2Kb or HLA-A2. Specifically, HLA-A2 transgenic mice were immunized subcutaneously in the footpad with 100 µg of p5 peptide together with 140 µg of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated *in vitro* with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary *in vitro*

stimulation. Retrovirally transduced cells expressing the control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were identified.

Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by culturing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, the DC were pulsed with p5 peptide and cultured with GM-CSF and IL-4 together with CD8+ T cell enriched PBMC. CTL lines were restimulated on a weekly basis with p5-pulsed monocytes. Five to six weeks after initiation of the CTL cultures, CTL recognition of p5-pulsed target cells was demonstrated.

#### EXAMPLE 11

##### EXPRESSION OF A BREAST TUMOR-DERIVED ANTIGEN IN PROSTATE

Isolation of the antigen B305D from breast tumor by differential display is described in US Patent Application No. 08/700,014, filed August 20, 1996. Several different splice forms of this antigen were isolated. The determined cDNA sequences for these splice forms are provided in SEQ ID NO: 366-375, with the predicted amino acid sequences corresponding to the sequences of SEQ ID NO: 292, 298 and 301-303 being provided in SEQ ID NO: 299-306, respectively.

The expression levels of B305D in a variety of tumor and normal tissues were examined by real time PCR and by Northern analysis. The results indicated that B305D is highly expressed in breast tumor, prostate tumor, normal prostate tumor and normal testes, with expression being low or undetectable in all other tissues examined (colon tumor, lung tumor, ovary tumor, and normal bone marrow, colon, kidney, liver, lung, ovary, skin, small intestine, stomach).



## EXAMPLE 12

### ELICITATION OF PROSTATE TUMOR ANTIGEN-SPECIFIC CTL RESPONSES IN HUMAN BLOOD

This Example illustrates the ability of a prostate tumor antigen to elicit a CTL response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GM-CSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8<sup>+</sup> cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles, CD8<sup>+</sup> lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL transduced to express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxicity assays (<sup>51</sup>Cr release) and interferon-gamma production (Interferon-gamma Elispot; see above and Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). The results of these assays are presented in Figures 6A and 6B.

## EXAMPLE 13

### IDENTIFICATION OF PROSTATE TUMOR ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of certain prostate tumor polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

Table I  
Summary of Prostate Tumor Antigens

Known Genes	Previously identified Genes	Novel Genes
T-cell gamma chain	P504S	23379 (SEQ ID NO:389)
Kallikrein	P1000C	23399 (SEQ ID NO:392)
Vector	P501S	23320 (SEQ ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID NO:385)	P503S	23381 (SEQ ID NO:390)
PSA	P510S	
Ald. 6 Dehyd.	P784P	
L-iditol-2 dehydrogenase (23376; SEQ ID NO:388)	P502S	
Ets transcription factor PDEF (22672; SEQ ID NO:398)	P706P	
hTGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ ID NO:396)	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang(23404; SEQ ID NO:393)	
Prostatic Acid Phosphatase(22655; SEQ ID NO:397)	P712P	
transglutaminase (22611; SEQ ID NO:395)	P778P	
HDLBP (23508; SEQ ID NO:394)		
CGI-69 Protein(23367; SEQ ID NO:387)		
KIAA0122(23383; SEQ ID NO:391)		
TEEG		

CGI-82 showed 4.06 fold over-expression in prostate tissues as

compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of

normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97% of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

#### EXAMPLE 14

##### IDENTIFICATION OF PROSTATE TUMOR ANTIGENS BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify prostate tumor antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatizis et al., *Proc. Natl. Acad. Sci. USA* 95:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped

(aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups, Plus (normal prostate and prostate tumor libraries, and breast cell lines, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

Table II  
Prostate cDNA Libraries and ESTs

Library	# of Libraries	# of ESTs
Plus	25	43,482
Normal	11	18,875
Tumor	11	21,769
Cell lines	3	2,838
Minus	166	
Other	287	

Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups: Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones found in the Plus and Other group libraries only; no expression detected in the Minus group; Type 3- EST clones found in the Plus, Minus and Other group libraries, but the

expression in the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones found in Plus, Minus and Other group libraries, but the expression in the Plus group is higher than the expression in the Minus group. This analysis identified 4,345 breast clusters (*see* Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

Table III  
Prostate Cluster Summary

Type	# of Superclusters	# of ESTs Ordered
1	688	677
2	2899	2484
3	85	11
4	673	0
Total	4345	3172

The inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

Clones with an expression ratio greater than 3 (*i.e.*, the level in prostate tumor cDNA was at least three times the level in normal prostate cDNA) were

identified as prostate tumor-specific sequences (Table IV). The sequences of these clones are provided in SEQ ID NOs:401-453, with certain novel sequences shown in SEQ ID NOs:407, 413, 416-419, 422, 426, 427 and 450.

Table IV  
Prostate-tumor Specific Clones

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1000C
402	22547	previously identified P704P
403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
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423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P



433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
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452	23618	previously identified P1000C
453	23622	previously identified P705P

#### EXAMPLE 15

#### FURTHER IDENTIFICATION OF PROSTATE TUMOR ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of additional prostate tumor polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NOs:454-467. Of these sequences SEQ ID NOs:459-461 correspond to novel genes. The others (SEQ ID NOs:454-458 and 461-467) correspond to known sequences.

## EXAMPLE 16

## FURTHER CHARACTERIZATION OF PROSTATE TUMOR ANTIGEN P710P

This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P fragment described above. One million colonies were plated on LB/Ampicillin plates. Nylon membrane filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic ABI Sequencer. Four sequences were obtained, and are presented in SEQ ID NOs:468-471.

From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for the purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the present invention is not limited except as by the appended claims.

## CLAIMS

1. An isolated polypeptide comprising at least an immunogenic portion of a prostate tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a) sequences recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472;

(b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and

(c) complements of any of the sequence of (a) or (b).

2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing polynucleotide sequences.

3. An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 108, 112, 113, 114, 172, 176, 178, 327, 329, 331, 339 and 383.

4. An isolated polynucleotide encoding at least 15 amino acid residues of a prostate tumor protein, or a variant thereof that differs in one or more

substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing sequences.

5. An isolated polynucleotide encoding a prostate tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing sequences.

6. An isolated polynucleotide comprising a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472.

7. An isolated polynucleotide comprising a sequence that hybridizes, under moderately stringent conditions, to a sequence recited in any one of

SEQ ID NOs: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472.

8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

9. An expression vector comprising a polynucleotide according to any one of claims 4-7.

10. A host cell transformed or transfected with an expression vector according to claim 9.

11. An expression vector comprising a polynucleotide according claim 8.

12. A host cell transformed or transfected with an expression vector according to claim 11.

13. A pharmaceutical composition comprising a polypeptide according to claim 1, in combination with a physiologically acceptable carrier.

14. A vaccine comprising a polypeptide according to claim 1, in combination with a non-specific immune response enhancer.

15. A vaccine according to claim 14, wherein the non-specific immune response enhancer is an adjuvant.

16. A vaccine according to claim 14, wherein the non-specific immune response enhancer induces a predominantly Type I response.

17. A pharmaceutical composition comprising a polynucleotide according to claim 4, in combination with a physiologically acceptable carrier.

18. A vaccine comprising a polynucleotide according to claim 4, in combination with a non-specific immune response enhancer.

19. A vaccine according to claim 18, wherein the non-specific immune response enhancer is an adjuvant.

20. A vaccine according to claim 18, wherein the non-specific immune response enhancer induces a predominantly Type I response.

21. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a prostate tumor protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472 or a complement of any of the foregoing polynucleotide sequences.

22. A pharmaceutical composition comprising an antibody or fragment thereof according to claim 18, in combination with a physiologically acceptable carrier.

23. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

24. A pharmaceutical composition according to claim 23, wherein the antigen presenting cell is a dendritic cell or a macrophage.

25. A vaccine comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a non-specific immune response enhancer.

26. A vaccine according to claim 25, wherein the non-specific immune response enhancer is an adjuvant.

27. A vaccine according to claim 25, wherein the non-specific immune response enhancer induces a predominantly Type I response.

28. A vaccine according to claim 25, wherein the antigen-presenting cell is a dendritic cell.

29. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a polypeptide according to claim 1, and thereby inhibiting the development of a cancer in the patient.

30. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a polynucleotide according to claim 4, and thereby inhibiting the development of a cancer in the patient.

31. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antibody or antigen-

binding fragment thereof according to claim 21, and thereby inhibiting the development of a cancer in the patient.

32. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide according to claim 1, and thereby inhibiting the development of a cancer in the patient.

33. A method according to claim 32, wherein the antigen-presenting cell is a dendritic cell.

34. A method according to any one of claims 29-32, wherein the cancer is prostate cancer.

35. A fusion protein comprising at least one polypeptide according to claim 1.

36. A fusion protein according to claim 35, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.

37. A fusion protein according to claim 35, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.

38. A fusion protein according to claim 35, wherein the fusion protein comprises an affinity tag.

39. An isolated polynucleotide encoding a fusion protein according to claim 35.



40. A pharmaceutical composition comprising a fusion protein according to claim 32, in combination with a physiologically acceptable carrier.

41. A vaccine comprising a fusion protein according to claim 35, in combination with a non-specific immune response enhancer.

42. A vaccine according to claim 41, wherein the non-specific immune response enhancer is an adjuvant.

43. A vaccine according to claim 41, wherein the non-specific immune response enhancer induces a predominantly Type I response.

44. A pharmaceutical composition comprising a polynucleotide according to claim 40, in combination with a physiologically acceptable carrier.

45. A vaccine comprising a polynucleotide according to claim 40, in combination with a non-specific immune response enhancer.

46. A vaccine according to claim 45, wherein the non-specific immune response enhancer is an adjuvant.

47. A vaccine according to claim 45, wherein the non-specific immune response enhancer induces a predominantly Type I response.

48. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 40 or claim 44.

49. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 41 or claim 45.

50. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i) polynucleotides recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472; and

(ii) complements of the foregoing polynucleotides;

wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the prostate tumor protein from the sample.

51. A method according to claim 50, wherein the biological sample is blood or a fraction thereof.

52. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 50.

53. A method for stimulating and/or expanding T cells specific for a prostate tumor protein, comprising contacting T cells with one or more of:

(i) a polypeptide according to claim 1;

(ii) a polypeptide encoded by a polynucleotide comprising a sequence provided in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472;

(iii) a polynucleotide encoding a polypeptide of (i) or (ii); and/or

(iv) an antigen presenting cell that expresses a polypeptide of (i) or (ii);

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

54. An isolated T cell population, comprising T cells prepared according to the method of claim 53.

55. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 54.

56. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with at least one component selected from the group consisting of:

(i) a polypeptide according to claim 1;

(ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472;

(iii) a polynucleotide encoding a polypeptide of (i) or (ii); or

(iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

57. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

- (a) incubating CD4<sup>+</sup> and/or CD8<sup>+</sup> T cells isolated from a patient with at least one component selected from the group consisting of:
- (i) a polypeptide according to claim 1;
  - (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472;
  - (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or
  - (iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);
- such that T cells proliferate;
- (b) cloning at least one proliferated cell; and
  - (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

58. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

- (a) contacting a biological sample obtained from a patient with a binding agent that binds to a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
  - (i) polynucleotides recited in any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472; and
  - (ii) complements of the foregoing polynucleotides;
- (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

59. A method according to claim 58, wherein the binding agent is an antibody.

60. A method according to claim 59, wherein the antibody is a monoclonal antibody.

61. A method according to claim 58, wherein the cancer is prostate cancer.

62. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472, or a complement of any of the foregoing polynucleotides;

(b) detecting in the sample an amount of polypeptide that binds to the binding agent;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

63. A method according to claim 62, wherein the binding agent is an antibody.

64. A method according to claim 63, wherein the antibody is a monoclonal antibody.

65. A method according to claim 62, wherein the cancer is a prostate cancer.

66. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472, or a complement of any of the foregoing polynucleotides;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

(c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

67. A method according to claim 66, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

68. A method according to claim 66, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

69. A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor

protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472, or a complement of any of the foregoing polynucleotides;

(b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

(c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

70. A method according to claim 69, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

71. A method according to claim 69, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

72. A diagnostic kit, comprising:

- (a) one or more antibodies according to claim 21; and
- (b) a detection reagent comprising a reporter group.

73. A kit according to claim 72, wherein the antibodies are immobilized on a solid support.

74. A kit according to claim 73, wherein the solid support comprises nitrocellulose, latex or a plastic material.

75. A kit according to claim 72, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

76. A kit according to claim 72, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.

77. An oligonucleotide comprising 10 to 40 nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing polynucleotides.

78. A oligonucleotide according to claim 77, wherein the oligonucleotide comprises 10-40 nucleotides recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472.

79. A diagnostic kit, comprising:

(a) an oligonucleotide according to claim 77; and

(b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.



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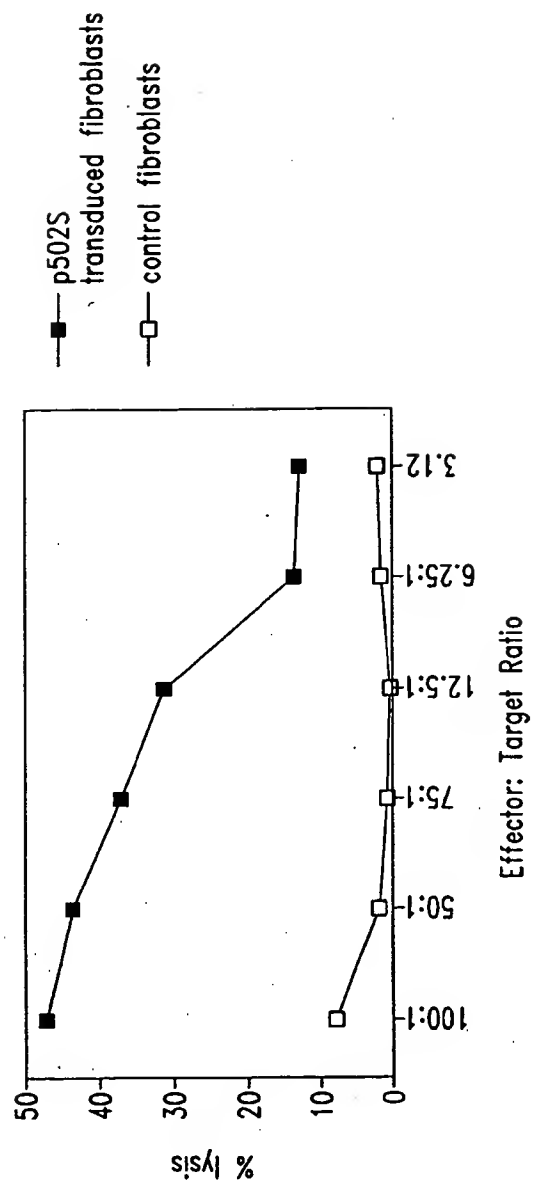
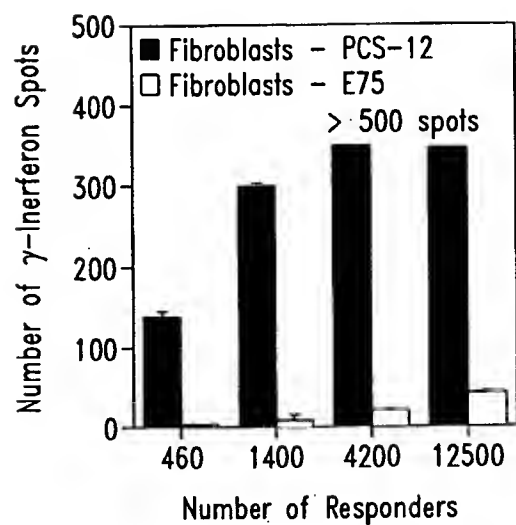
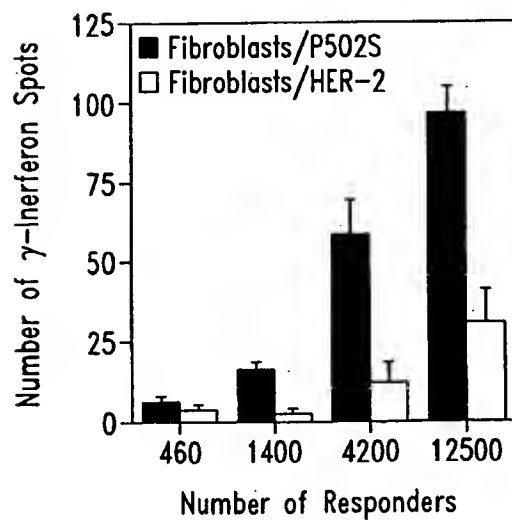


Fig. 1

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*Fig. 2A**Fig. 2B*

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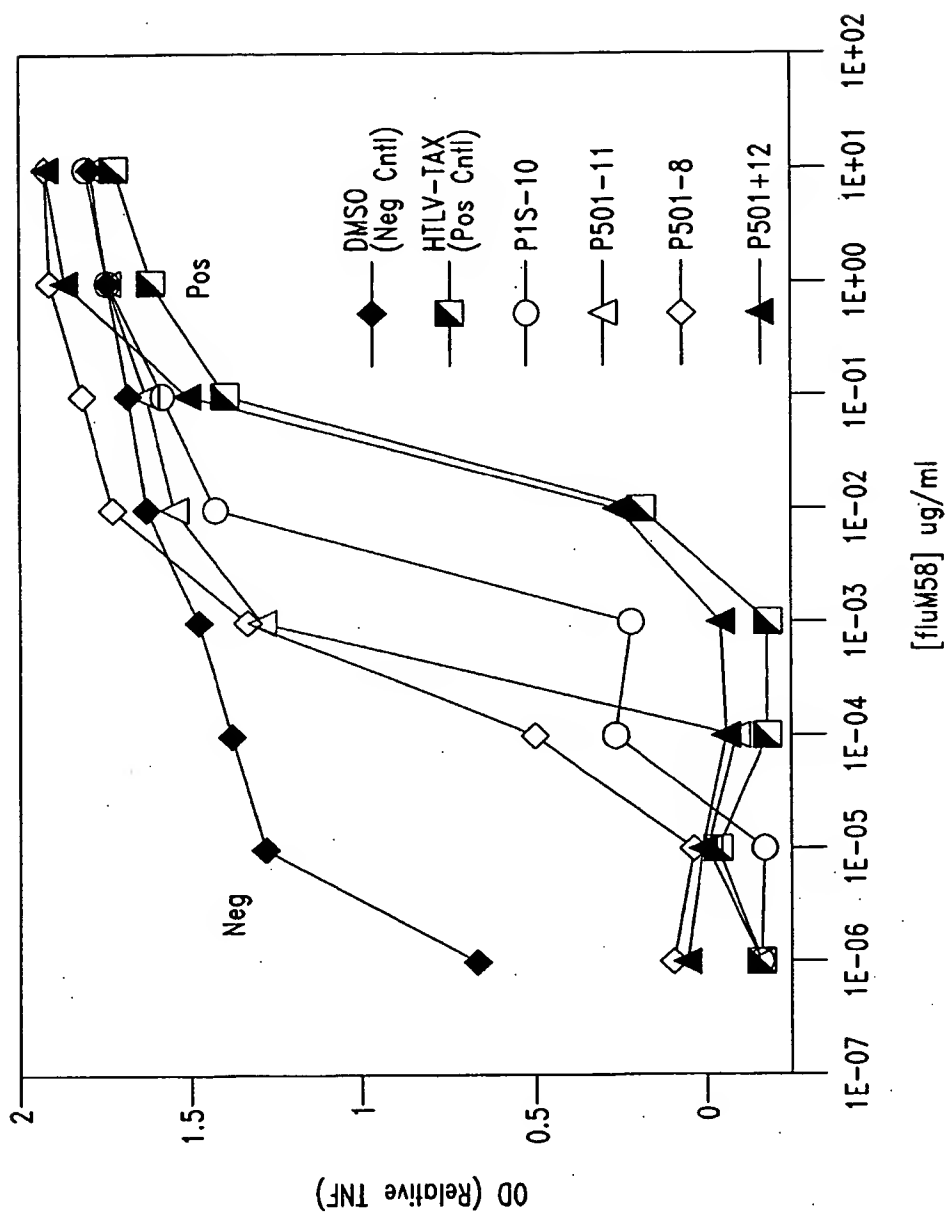
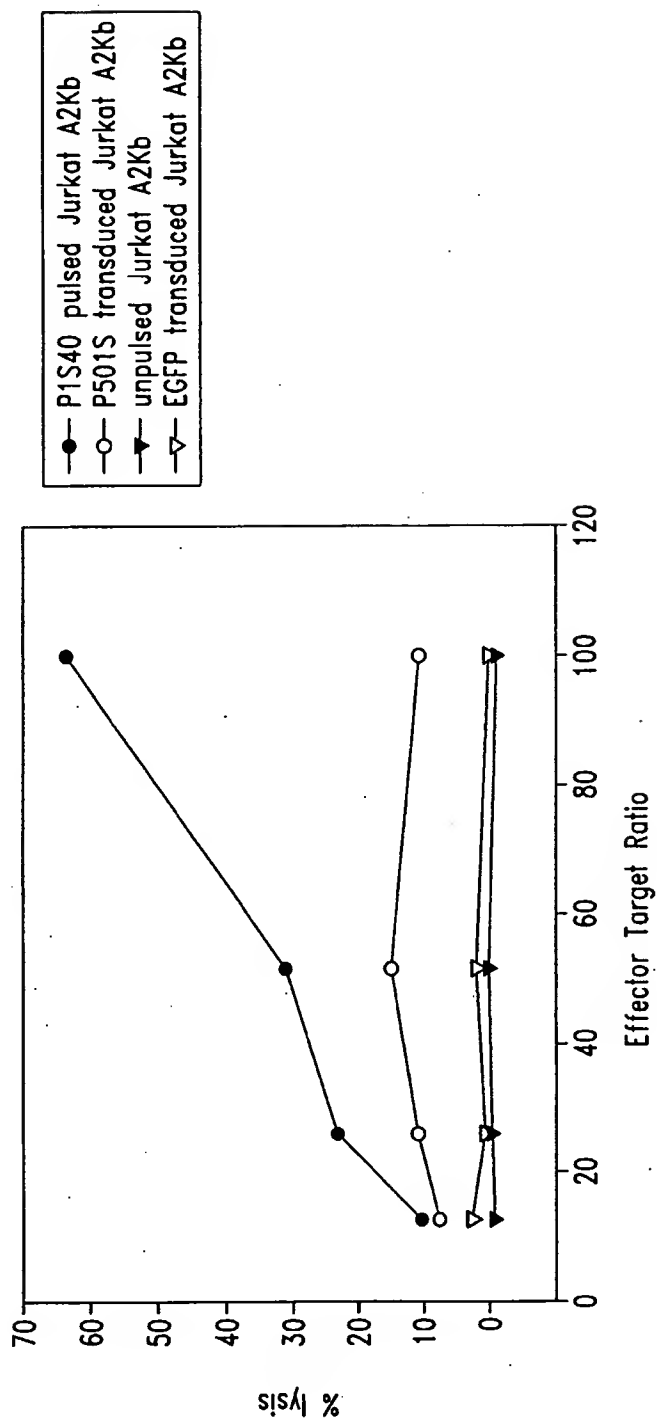


Fig. 3

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*Fig. 4*

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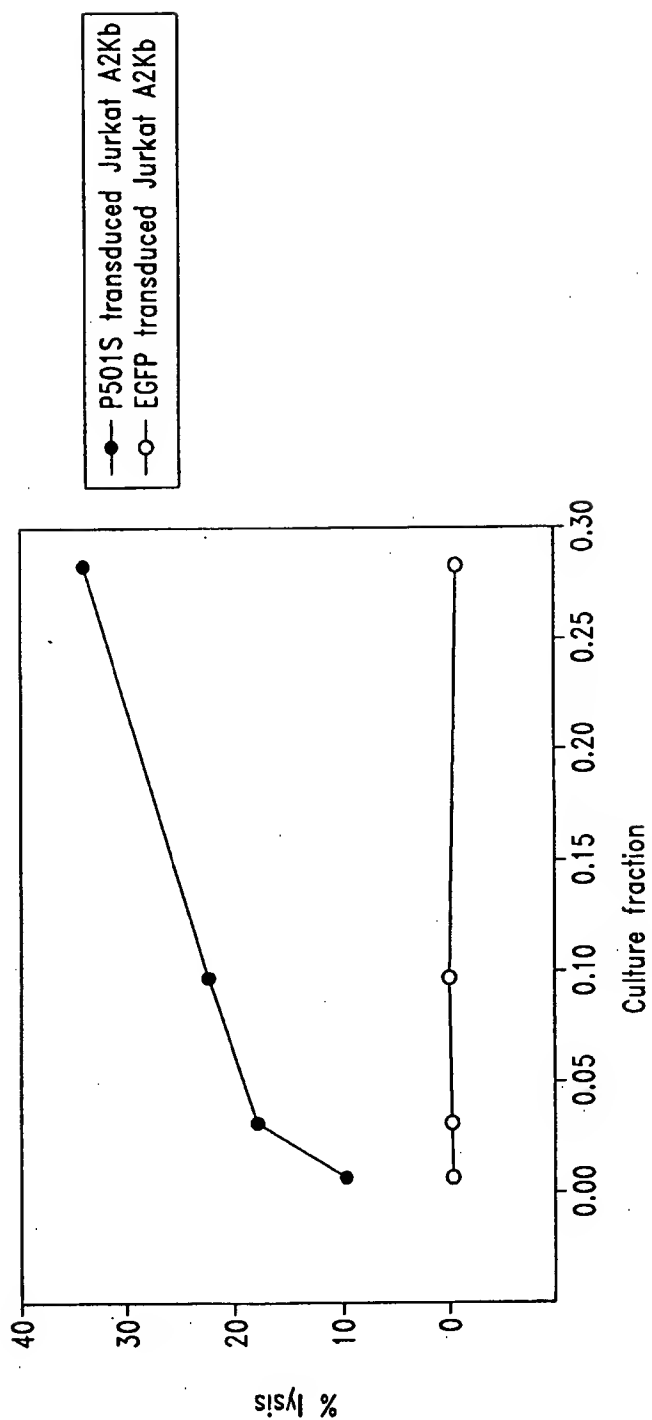
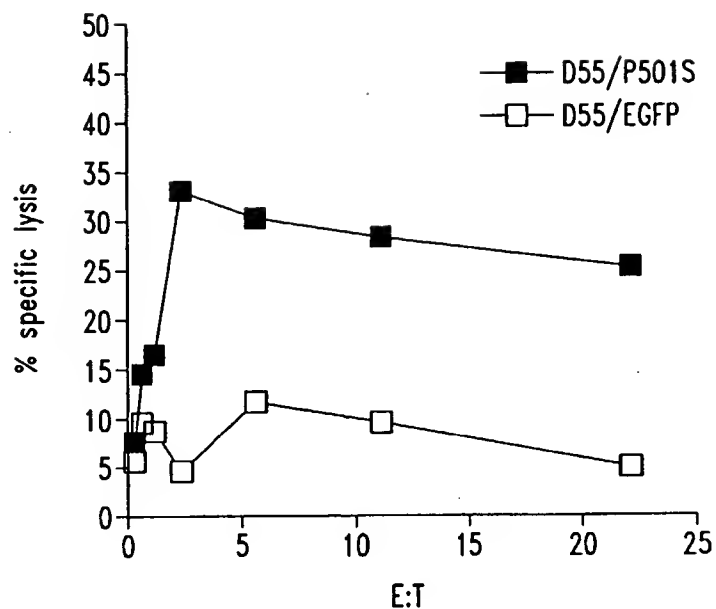
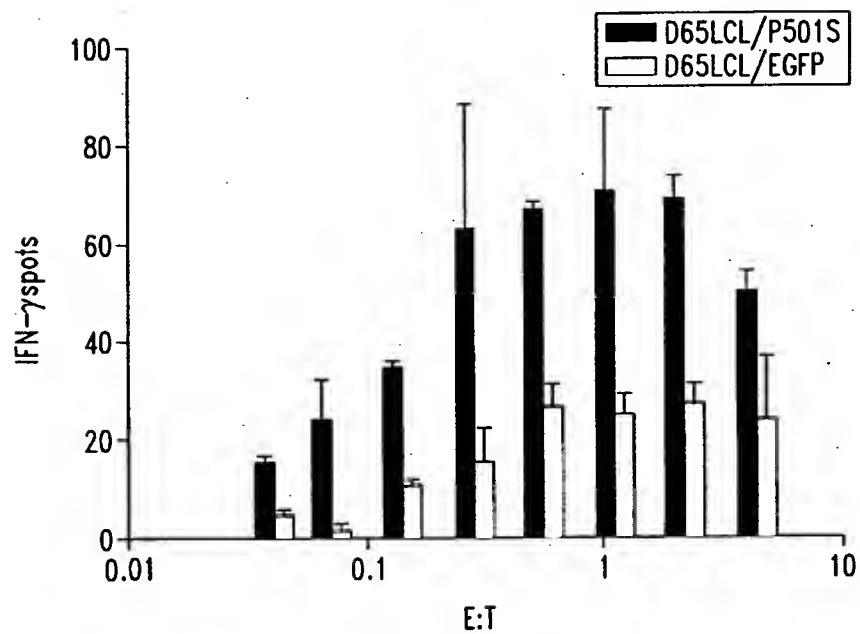


Fig. 5

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*Fig. 6A**Fig. 6B*

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<120> COMPOSITIONS AND METHODS FOR THE THERAPY AND  
DIAGNOSIS OF PROSTATE CANCER

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ctgctgttaa	acaccccagc	catcccttct	ttcaaaaggg	atccactagt	tctagaagcg	420
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ggcgtaatca	tgggtcatagc	tgtttcctgt	gtgaaattgt	tatccgctca	caattccccc	540
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tcgctcattg	atcctngcnc	ccggtcttcg	gctgcggnga	acggttcaact	cctcaaaggc	780
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<210> 3  
 <211> 773  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(773)  
 <223> n = A,T,C or G

<400> 3						
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tcctcaaaag	tcagaaccgg	agtcacacag	gcattctgtg	cgtaaaagat	ttgacaccac	180
tctgccttcg	tcttctttgc	aaatacatct	gcaaacttct	tcttcatttc	tggccaatca	240
tccatgtca	tctgattggg	aagttcatca	gactttagtc	canntccttt	gatcagcagc	300
tcgtagaact	ggggttctat	tgtccaaca	gccatgaatt	ccccatctgc	tgtcctgtaa	360
gtcgtataga	aaggtgctcc	accatccaac	atgttctgtc	ctcgaggggg	ggcccggtac	420
ccaattcgcc	ctatantgag	tcgtattacg	cgcgctcaact	ggccgctcgtt	ttacaacgtc	480
gtgactggga	aaaccttggg	cgttaccaac	ttaatcgctt	tgcagcacat	ccccctttcg	540
ccagctgggc	gtaatanoga	aaaggccgc	accgatcgcc	ctccaacag	ttgcgcacct	600
gaatgggnaa	atgggacccc	cctgttacgg	cgcattnaac	ccccgcnggg	tttngttgtt	660
acccccacnt	nnaccgctta	cactttgcca	gcgccttanc	gcccgtccc	tttcnctttt	720
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<210> 4  
 <211> 828  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(828)  
 <223> n = A,T,C or G

<400> 4						
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acgtgggtga	ccatgttgtt	tgtgggggtgc	agagatggga	ggggtggggc	ccaccctgga	240
agagtggaca	gtgacacaag	gtggacactc	tctacagatc	actgaggata	agctggagcc	300
acaatgcatg	aggcacacac	acagcaagga	tgacnctgta	aacatagccc	acgtgtcct	360
gnngggcactg	ggaagcctan	atnaggccgt	gagcanaaag	aaggggagga	tccactagtt	420
ctanagcggc	cgcaccgcg	gtgganctcc	ancttttgtt	cccttttagtg	agggttaatt	480
gcgcgcttgg	cntaatcatg	gtcatanctn	tttcctgtgt	gaaattgtta	tccgctcaca	540
attccacaca	acatacganc	cggaacata	aantgtaaac	ctgggggtgcc	taatgantga	600
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ccncttgcat	tnatgaatcn	gccaaacccc	ggggaaaagc	gtttgcgttt	tgggcgctct	720
tccgcttctc	cnctcantta	ntccctncnc	tcggtcattc	cggctgcngc	aaaccggttc	780
accnctcca	aaggggggtat	tccggtttcc	ccnaatccgg	gganance		828

<210> 5  
 <211> 834  
 <212> DNA  
 <213> Homo sapien



<220>  
 <221> misc\_feature  
 <222> (1)...(834)  
 <223> n = A,T,C or G

<400> 5

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attttataac	aatcaacacc	tgtggctttt	aaaatttgg	tttcataaga	taattttatac	180
tgaagtaaat	ctagccatgc	ttttaaaaaa	tgcttttaggt	cactccaagc	ttggcagtta	240
acatttggca	taaacaataa	taaaacaatc	acaatttaat	aaataacaaa	tacaacattg	300
taggccataa	tcatatagag	tataaggaaa	aggtggtagt	gttgagtaag	cagttattag	360
aatagaatac	cttggcctct	atgcaaatat	gtctagacac	tttgattcac	tcagccctga	420
cattcagttt	tcaaagtagg	agacagggtc	tacagtatca	ttttacagtt	tccaacacat	480
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tcaccaaccc	ctcagttata	aaaaattttc	aagtatatatt	agtcataata	cttgggtgtgc	600
ttattttaaa	ttagtgtctaa	atggatttaag	tgaagacaac	aatgggtcccc	taatgtgatt	660
gatatttggtc	atttttacca	gcttctaaat	ctnaactttc	aggcttttga	actggaacat	720
tgnatnacag	tgttccanag	ttncaaccta	ctggaacatt	acagtgtgct	tgattcaaaa	780
tgttattttg	ttaaaaatta	aattttaacc	tggtggaaaa	ataatttgaa	atna	834

<210> 6  
 <211> 818  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(818)  
 <223> n = A,T,C or G

<400> 6

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tgtaaagtga	aatattagtt	ggcggatgaa	gcagatagtg	aggaaagtgt	agccaataat	180
gacgtgaagt	ccgtggaagc	ctgtggctac	aaaaaatggt	gagccgtaga	tgccgtcgga	240
aatgggtgaag	ggagactcga	agtactctga	ggcttgtagg	agggtaaaaat	agagaccag	300
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gtgagctcag	gtgattgata	ctcctgatgc	gagtataacg	gatgtgttta	ggagtgggac	420
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aggggctagg	ctggagtggg	aaaaggctca	gaaaaatcct	gcgaagaaaa	aaacttctga	540
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ttggtatgtg	ctttctcgtg	ttacatcgcg	ccatcattgg	tatatgggta	gtgtgttggg	660
ttantangg	ctantatgaa	gaacttttgg	antggaatta	aatcaatngc	ttggccggaa	720
gtcattanga	nggctnaaaa	ggccctgtta	ngggtctggg	ctnggtttta	cccnaccat	780
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<210> 7  
 <211> 817  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(817)  
 <223> n = A,T,C or G

<400> 7

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ggtttgctac	acagatttca	gagcattgac	cgtagtatac	ccccggtcgt	gtagcgggtga	180

aagtggtttg	gttttagacgt	ccggaattg	catctgtttt	taagccta	gtggggacag	240
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gtactactcg	attgtcaacg	tcaaggagtc	gcaggtcgcc	tggttctagg	aataatgggg	360
gaagtatgta	ggaattgaag	attaatccgc	cgtagtcggt	gttctcctag	gttcaatacc	420
attggtggcc	aattgatttg	atggtaagg	gagggatcgt	tgaactcgtc	tgttatgtaa	480
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gaatnttng	gaaaagggct	tacaggacta	gaaaccaa	angaaaanta	atnntaangg	660
cnttatcntn	aaaggnata	accnctccta	tnatccacc	caatngnatt	ccccacnenn	720
acnattggat	nccccanttc	canaaaangc	cnccecccg	tgnannccnc	cttttgttcc	780
cttnantgan	ggttattcnc	ccctngcntt	atcance			817

&lt;210&gt; 8

&lt;211&gt; 799

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(799)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 8

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ctccttacaa	ccacannatg	cccggctcct	cccggaaacc	antccancc	tgngaaggat	540
caagnccctgn	atccactnnt	nctanaaccg	gccnccnccg	cngtggaaac	cnccttntgt	600
tccctttcnt	tnagggttaa	tnnccgcttg	gccttnccan	ngtccctncn	nttttccnnt	660
gttnaaattg	ttangcnccc	nccnntcccn	cnnnnnnan	cccgaaccnn	annttnnann	720
ncctgggggt	ncnncngat	tgaccenncc	nccctntant	tgcnttnggg	nnnntgccc	780
ctttccctct	nggganncg					799

&lt;210&gt; 9

&lt;211&gt; 801

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(801)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 9

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taangatgac	actcccaaag	gtggtcctga	cagtggccca	gatggacatg	gggctcacct	120
caaggacaag	gccaccaggt	gcgggggccc	aagcccacat	gacccctact	ctatgagcaa	180
aatccctgtg	gggggcttct	ccttgaagtc	cgccancagg	gctcagtctt	tggaccang	240
caggtcatgg	ggttgtnngc	caactggggg	ccncaacgca	aaanggcnc	gggcctcngn	300
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cncntantg	caccnattec	caenttttnc	agntttccnc	nnccngcttc	cttntaaaag	540
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gctgaantcc	ccatnaccnn	gnctcnatgg	anccntccnt	tttaannacn	ttctnaactt	660
gggaananc	ctcgnccntn	ccccnttaa	tccnccctg	cnangnncnt	ccccnntcc	720
nccnnntng	gcntntnann	cnaaaaaggc	ccnnnanc	tctcctnn	cctcanttgc	780

ccanccctcg aaatcgccn c

801

<210> 10  
 <211> 789  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(789)  
 <223> n = A,T,C or G

<400> 10  
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 agatcctgcc ctacacactg gcctccctct accaccggga gaagcaggtg ttcctgccc 180  
 aataccgagg ggacactgga ggtgctagca gtgaggacag cctgatgacc agcttcctgc 240  
 caggccctaa gcctggagct ccctcccta atggacacgt ggggtgctgga ggcagtggcc 300  
 tgctcccacc tccaccgag ctctgagggg cctctgcctg tgatgtctcc gtacgtgtgg 360  
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 ccatcctgga tagtgcttcc tgctgtccca ngtggcccca tccctgttta tgggctccat 480  
 tgtccagctc agccagtctg tcaactgccta tatggtgtct gccgcaggcc tgggtctggt 540  
 cccatttact ttgctacaca ggtantattt gacaagaacg anttggccaa atactcagcg 600  
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 tcctgttaac cccatggggc tgccggcttg gccgccaatt tctgttgctg ccaaantnat 720  
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 gnggttccc 789

<210> 11  
 <211> 772  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(772)  
 <223> n = A,T,C or G

<400> 11  
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 accaacaggc cacatcctga taaaaggtaa gaggggggtg gatcagcaaa aagacagtgc 180  
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 actttcatat gttcaaatcc catggaggag tgtttcatcc tagaaactcc catgcaagag 300  
 ctacattaaa cgaagctgca ggttaagggg ctanagatg ggaaaccagg tgactgagtt 360  
 tattcagctc ccaaaaaccc ttctctaggt gtgtctcaac taggaggcta gctgttaacc 420  
 ctgagcctgg gtaatccacc tgcagagtcc ccgcattcca gtgcatgga ccttctggc 480  
 ctccctgtat aagtccagac tgaaaccccc ttggaaggnc tccagtcagg cagccctana 540  
 aactggggaa aaaagaaaag gacgccccan cccccagctg tgcanctacg cacctcaaca 600  
 gcacaggggtg gcagcaaaaa aaccacttta ctttggcaca aacaaaaact ngggggggca 660  
 accccggcac cccnangggg gttaacagga ancngggnaa cntggaaccc aattnaggca 720  
 ggccnccac ccnaatntt gctgggaaat ttttctccc ctaaattntt tc 772

<210> 12  
 <211> 751  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(751)  
 <223> n = A,T,C or G

&lt;400&gt; 12

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ttggctgtgt	tggtgacgtt	gtcattgcaa	cagaatgggg	gaaaggcact	gttctctttg	180
aagtanggtg	agtcctcaaa	atccgtatag	ttggtgaagc	cacagcactt	gagccctttc	240
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agcagctgcn	acctcagcaa	tgaagatgan	gaggangatg	aagaagaacg	tcncgagggc	420
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agtggcccna	aaaatcttca	aaaaggatgc	cccatcnatt	gaccccccaa	atgccactg	600
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tnatnaacnt	gaacctgcn	tngtggctcc	tgttcaggnc	cnnggcctga	cttctnaann	720
aangaactcn	gaagncccca	cngganannc	g			751

&lt;210&gt; 13

&lt;211&gt; 729

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1)...(729)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 13

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accatgcagt	gcttcagctt	cattaagacc	atgatgatcc	tcttcaattt	gctcatcttt	180
ctgtgtgggtg	cagccctgtt	ggcagtgggc	atctgggtgt	caatcgatgg	ggcatccttt	240
ctgaagatct	tcgggccact	gtcgtcca	gcatgcagt	ttgtcaacgt	gggctacttc	300
ctcatcgcat	ccggcggtgt	ggtcttagct	ctagggttcc	tgggctgcta	tgggtgctaag	360
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gaagantcac	ctacttcaaa	gaaaanagt	cctttccccc	atttctgttg	caattgacaa	660
acgtcccaa	cacagccaat	tgaaaacctg	cacccaaccc	aaanggggtcc	ccaaccanaa	720
attnaaggg						729

&lt;210&gt; 14

&lt;211&gt; 816

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1)...(816)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 14

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ggcagggtcca	cgcagtgcc	ttgtcactg	gggaaatgga	tgcgctggag	ctcgtcaaa	180
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tganccccan	anctgcctct	caaangcccc	accttgacac	ccccgacagg	ctagaatgga	420
atcttcttcc	cgaaggtag	ttnttcttgt	tgcccaancc	anccccntaa	acaaactctt	480
gcanatctgc	tcgnggggg	tcntantacc	ancgtgggaa	aagaacccca	ggcngcgaa	540
caancttgtt	tgatnccgaa	gcnataatct	ncntttctgc	ttggtggaca	gcaccantna	600

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cncnctccta	ccccagaaan	nccgtgttcc	cccccaacta	ggggccnaaa	ccnntttttc	780
cacaaccctn	ccccaccac	gggttcngnt	ggttng			816

<210> 15  
 <211> 783  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(783)  
 <223> n = A,T,C or G

<400> 15						
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aagacccaaa	ccaggtggaa	ctgtggggac	tcaaggaang	cacctacctg	ttccagctga	180
cagtgaactag	ctcagaccac	ccagaggaca	cggccaacgt	cacagtcaact	gtgctgtcca	240
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gcttgggcaa	caagaacaac	taccttcggg	aagaagagtg	cattctancc	tgtcnggggtg	420
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ccatggaaag	gcgccatcca	ntgttctctg	gcacctgtca	gcccaccag	ttccgctgca	540
ncaatggctg	ctgcatcnac	antttcctng	aattgtgaca	acaccccca	ntgcccccaa	600
ccctcccaac	aaagcttccc	tgtnnaaaaa	tacnccantt	ggcttttnac	aaacnccgg	660
cncctcctt	ttcccnntn	aacaaagggc	nctngcnttt	gaactgccc	aaccnggaa	720
tctnccnng	aaaaantncc	ccccctggtt	cctnnaance	cctccncaa	antncccc	780
ccc						783

<210> 16  
 <211> 801  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(801)  
 <223> n = A,T,C or G

<400> 16						
gccccaatc	cagctgccac	accacccacg	gtgactgcat	tagttcggat	gtcatacaaa	60
agctgattga	agcaaccctc	tacttttttg	tcgtgagcct	tttgcctggt	gcaggtttca	120
ttggctgtgt	tggtgacgtt	gtcattgcaa	cagaatggg	gaaaggcact	gttctctttg	180
aagtaggggtg	agtcctcaaa	atccgtatag	ttgggtgaagc	cacagcactt	gagccctttc	240
atggtgggtg	tccacacttg	agtgaagtct	tcctgggaac	cataatcttt	cttgatggca	300
ggcactacca	gcaacgtcag	gaagtgtcga	gccattgtgg	tgtacaccaa	ggcgaccaca	360
gcagctgcaa	cctcagcaat	gaagatgagg	aggaggatga	agaagaacgt	cncgagggca	420
cacttgctct	ccgtcttagc	accatagcag	cccangaaac	caagagcaaa	gaccacaacg	480
ccngctgcga	atgaaagaaa	ntaccacagt	tgacaaactg	catggccact	ggacgacagt	540
tgggccgaan	atcttcagaa	aagggatgcc	ccatcgattg	aacaccana	tgccactgc	600
cnacagggtc	gcncncncn	gaaagaatga	gccattgaag	aaggatcntc	ntggtcttaa	660
tgaactgaaa	ccntgcatgg	tgggccctgt	tcagggtctc	tggcagtga	ttctganaaa	720
aaggaacngc	ntnagcccc	ccaaangana	aaacaccccc	gggtgttgcc	ctgaattggc	780
ggccaaggan	ccctgcccc	g				801

<210> 17  
 <211> 740  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(740)  
 <223> n = A,T,C or G

<400> 17  
 gtgagagcca ggcgtccctc tgcctgccca ctcaagtggca acacccggga gctgttttgt 60  
 cctttgtgga gcctcagcag ttccctcttt cagaactcac tgccaagagc cctgaacagg 120  
 agccaccatg cagtgtctca gcttcattaa gaccatgatg atcctcttca atttgctcat 180  
 ctttctgtgt ggtgcagccc tgttggcagt gggcatctgg gtgtcaatcg atggggcatc 240  
 ctttctgaag atcttcgggc cactgtcgtc cagtgccatg cagtttgtca acgtgggcta 300  
 cttectcatc gcagccggcg ttgtggctct tgccttgggt ttcctgggct gctatggtgc 360  
 taagacggag agcaagtgtg ccctcgtgac gttcttcttc atcctcctcc tcactcttcat 420  
 tgcgtgaagt gcagctgctg tgggtcgctt ggtgtacacc acaatggctg aaccattcct 480  
 gacgttgctg gtantgcctg ccatcaanaa agattatggg ttcccaggaa aaattcactc 540  
 aantntggaa caccnccatg aaaagggctc caatttctgn tggttccccc aactataccg 600  
 gaattttgaa agantcncct tacttccaaa aaaaaanant tgccttttnc ccntttctgt 660  
 tgcaatgaaa acntcccaan acngccaatn aaaacctgcc cnnncaaaaa ggnctcncaa 720  
 caaaaaaant nnaagggttn 740

<210> 18  
 <211> 802  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(802)  
 <223> n = A,T,C or G

<400> 18  
 ccgctgggtg cgctgggtcca gngnagccac gaagcacgtc agcatacaca gcctcaatca 60  
 caaggtcttc cagctgccgc acattacgca gggcaagagc ctccagcaac actgcatatg 120  
 ggatacactt tacttttagca gccagggtga caactgagag gtgtcgaagc ttattcttct 180  
 gagcctctgt tagtggagga agattccggg cttcagctaa gtatgcagcg tatgtcccat 240  
 aagcaaacac tgtgagcagc cggaaggtag aggcaaatgc actctcagcc agctctctaa 300  
 cattgggcat gtccagcagt tctccaaaaca cgtagacacc agnggcctcc agcacctgat 360  
 ggatgagtgt ggccagcgct gccccttgg ccgacttggc taggagcaga aattgtcct 420  
 ggttctgccc tgtcaccttc acttccgcac tcatcactgc actgagtgtg ggggacttgg 480  
 gctcaggatg tccagagacg tggttccgcc ccctcnctta atgacaccgn ccanncaacc 540  
 gtcggctccc gccgantgng ttcgtcgtnc ctgggtcagg gtctgctggc cncacttgc 600  
 aancttctgc nggcccattg aattcaccnc accggaactn gtangatcca ctnnttctat 660  
 aaccgngcgc caccgcnntt ggaactccac tcttnttnc tttacttgag ggttaaggct 720  
 acccttnnccg ttactttggt ccaaacctn cctgtgtcgt anantngtnaa tcnggnccna 780  
 tnccanccnc atangaagcc ng 802

<210> 19  
 <211> 731  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(731)  
 <223> n = A,T,C or G

<400> 19  
 cnaagcttcc aggtnacgg cgcnaancc tgacccnagg tancanaang cagnncgcgg 60  
 gagcccaccg tcacngngng gngtctttat nggagggggc ggagccacat cnetggacnt 120  
 cntgaccca actcccncc ncncantgca gtgatgagt cagaactgaa ggtnacgtgg 180  
 caggaaccaa gancaaannc tgctccnntc caagtccgn nagggggcgg ggctggccac 240  
 gncatccnt cnagtgtgn aaagcccnac cctgtctact tgtttggaga acngcnnga 300

```

catgccagn gttanataac nggcngagag tnannttgcc tctcccttcc ggctgcgcan 360
cgngtntgct tagnggacat aacctgacta cttaactgaa cccnngaate tncnccccct 420
ccactaagct cagaacaaaa aacttcgaca ccactcantt gtcacctgnc tgctcaagta 480
aagtgtaccc catncccaat gtntgctnga ngctctgncc tgcnttangt tgggtcctgg 540
gaagacctat caattnaagc tatgtttctg actgcctctt gctccctgna acaancnacc 600
cnncnntcca aggggggggnc ggcccccaat ccccccaacc ntnaattnan tttanccccn 660
ccccnggcc cggcctttta cnancntcnn nnacngggna aaaccnnngc tttncccaac 720
nnaatccncc t 731

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<210> 20
<211> 754
<212> DNA
<213> Homo sapien

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<220>
<221> misc feature
<222> (1)...(754)
<223> n = A,T,C or G

```

```

<400> 20
tttttttttt tttttttttt taaaaacccc ctccattnaa tgnaaacttc cgaaattgtc 60
caacccccctc ntccaaatnn ccntttccgg gnggggggttc caaacccaan ttanntttgg 120
annntaaatt aaatnttntt tggnggnnna anccnaatgt nangaaagt naaccanta 180
tnancttnaa tncctggaaa ccngtngntt ccaaaaatnt ttaaccctta antccctccg 240
aaatngttna nggaaaaccc aantttctnt aaggttggtt gaaggntnaa tnaaaanccc 300
nnccaattgt tttngccac gcctgaatta attggnntcc gntgttttcc nttaaaanaa 360
ggnnancccc ggttantnaa tcccccnnc cccaattata ccganttttt ttngaattgg 420
gancccnccg gaattaacgg ggnnnntccc tnttgggggg cnggnncccc cccntcggg 480
ggttngggnc aggncnnaat tgtttaaggg tccgaaaaat ccctcnaga aaaaaanctc 540
ccagngtgag nntnggggtt ncccccccc canggccct ctcgnanagt tgggggttg 600
ggggcctggg atttntttc cctnttnc tcccccccc ccnggganag aggttngngt 660
ttgtntcnn ggccccnccn aagantttt ccganttnan ttaaatecnt gcctnggcga 720
agtccttgn agggntaaan ggccccctnn cggg 754

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<210> 21
<211> 755
<212> DNA
<213> Homo sapien

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<220>
<221> misc feature
<222> (1)...(755)
<223> n = A,T,C or G

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```

<400> 21
atcancccat gacccnaac nngggaccnc tcanccggnc nnncnaccnc cgcccnatca 60
nngtnagnnc actncnnttn natcacnccc cncnactac gcccncnanc cnacgcncta 120
nncanatncc actganngcg cgangtngan ngagaaanct nataccanag ncaccanacn 180
ccagctgtcc nanaangcct nnnatacngg nnnatccaat ntgnanctc cnaagtattn 240
nncnncanat gattttcctn anccgattac cntncccc tanccctcc ccccaacna 300
cgaaggcnet ggnccnaagg nngcgnccc ccgctagntc cccnnaagt cncnnccta 360
aactcanccn nattaacncc ttentgagta tcaactcccc aatctcacc tactcaactc 420
aaaaanaton gatcaaaaat aatncaagcc tgnntatnac actntgactg ggtctctatt 480
ttagnngtcc ntnaancntc ctaatacttc cagtctncc tcnccaattt ccnaangget 540
ctttcngaca gcatntttt gttcccnntt gggttcttan ngaattgcc ttentngaac 600
gggctcntct tttccttcgg ttancctggg ttcnccggc cagttattat tccccnttt 660
aaattcntnc cntttanttt tggcnttcna aacccccggc cttgaaaacg gccccctggt 720
aaaaggttgt tttganaaaa tttttgtttt gttcc 755

```

```

<210> 22
<211> 849
<212> DNA

```

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)... (849)

<223> n = A,T,C or G

<400> 22

tttttttttt	tttttangtg	tngtctgtgca	ggtagagget	tactacaant	gtgaanacgt	60
acgctnggan	taangcgacc	cganttctag	ganncnccct	aaaatcanac	tgtgaagatn	120
atcctgnnna	cggaanggtc	accggnggat	nntgctaggg	tgncnctcc	cannncnttn	180
cataactcng	nggccctgcc	caccaccttc	ggcggcccg	ngnccgggcc	cgggtcattn	240
gnnttaaccn	cactnngcna	ncggtttccn	ncccnncng	accnngcgga	tccggggtnc	300
tctgtcttcc	cctgnagncn	anaaantggg	ccnccgnccc	ctttaccctt	nnacaagcca	360
cngcctteta	ncnccngccc	cccctccant	nngggggact	gccnanngt	ccgttntctng	420
nnaccccnnn	gggtncctcg	gttgctcgant	cnaccgnang	ccanggatcc	cnaaggaagg	480
tgcgttnttg	gccccctacc	tctcgtncgg	nncaccttc	ccgacnanga	nccgctccc	540
cnccnccngn	cctcncctcg	caacacccgc	ntctntcngt	ncggnnnccc	ccccaccgc	600
ncctcncnc	ngnccgnancn	ctccnccncc	gtctcannca	ccaccccgcc	ccgccagggc	660
ntcanccacn	ggngacnng	nagcncntc	gcnccgcgcn	gcgnccctt	cgccnngaa	720
ctnctcngg	ccantnnccg	tcaanccnna	cnaaacgcgc	ctgcgcggcc	cgnagcgnc	780
ncctccncca	gtcctcccgn	cttccnacc	angnntccn	cgaggacacn	nnaccccgcc	840
nnccangcgg						849

<210> 23

<211> 872

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)... (872)

<223> n = A,T,C or G

<400> 23

gcgcaaaacta	tacttcgctc	gnactcgtgc	gcctcgtcnc	tcttttcctc	cgcaaccatg	60
tctgacnanc	ccgattnggc	ngatatacnan	aagntcganc	agtccaaact	gantaacaca	120
cacacncnan	aganaaatcc	ntcgccttcc	anagtanaen	attgaacnng	agaaccangc	180
nggcgaatcg	taatnaggcg	tgcgcgcgca	atntgtcncc	gtttattntn	ccagctcnc	240
ctnccnacc	tactctctcn	nagctgtcnn	acccctngtn	cgnaccccc	naggtcggga	300
tccgggtttn	nntgaccng	cncccttcc	ccccctccat	nacganccnc	ccgcaccacc	360
nanngcnccg	nccccgnnet	cttcgcncnc	ctgtcctntn	ccctgtngc	ctggcnccgn	420
accgcattga	ccctcgccnn	ctnccnngaaa	ncgnanacgt	ccgggttggn	annancgctg	480
tgggnnngcg	tctgcncgc	gttccttccn	ncncttcca	ccatcttct	tacnggggtc	540
ccnccgctc	tccnnccacn	cctgggacgc	tntcctntgc	ccccctnac	tccccctt	600
cgncgtgncc	cgccccacc	ntcatttnca	nacgntcttc	acaannncct	ggntnnctcc	660
cnancngncc	gtcancnag	ggaagggngg	ggnnccnntg	nttgacgtg	nggngangtc	720
cgaanantcc	tccnccnccn	cnctaccctt	cgggcgnnet	ctcngttncc	aacttancaa	780
ntctcccccg	ngngcncntc	tcagcctcnc	ccncccnct	ctctgcantg	tntctcgtc	840
tnaccnntac	gantnttcgn	cncctcttt	cc			872

<210> 24

<211> 815

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)... (815)

<223> n = A,T,C or G

<400> 24



gcatgcaagc	ttgagtattc	tatagngtca	cctaaatanc	ttggcntaat	catggctenta	60
nctgncttcc	tgtgtcaaat	gtatacnaa	tanatatgaa	tctnatntga	caaganngta	120
tentncatta	gtaacaantg	tnntgtccat	cctgtengn	canattccca	tnnattncgn	180
cgcattcnen	gcncantatn	taatngggaa	ntcnntnnn	ncacnncat	ctatcntncc	240
gcncctgac	tggnagagat	ggatnanttc	tnntntgacc	nacatgttca	tcttggattn	300
aanancccc	cgngnccac	cggttngnng	cnagccnntc	ccaagacctc	ctgtggaggt	360
aacctgcgtc	aganncatca	aacntgggaa	acccgcnncc	angtnnaagt	ngnnncanan	420
gatcccgtec	aggnntnacc	atcccttcnc	agcgccccct	ttngtgcctt	anagnnagc	480
gtgtccnanc	cncatcaacat	ganacgcgcc	agnccanccg	caattnggca	caatgtcgnc	540
gaaccccccta	gggggantna	tncaaanccc	caggattgtc	cncncangaa	atcccnanc	600
ccnccctac	ccncttttg	gacngtgacc	aantcccga	gtncagtc	ggcngnctc	660
ccccaccggt	nnccntggg	gggtgaanct	cngnntcanc	cngncgaggn	ntcgnaagga	720
accggnccn	ggncgaanng	ancnntcnga	agnccnntc	cgtataacc	cccctcncca	780
ncnancngnt	agntcccc	cngggtncgg	aang			815

<210> 25  
 <211> 775  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(775)  
 <223> n = A,T,C or G

<400> 25						
ccgagatgtc	tcgctccgtg	gccttagctg	tgetcgcgt	actctctctt	tctggcctgg	60
aggctatcca	gcgtactcca	aagattcagg	tttactcacg	tcattccagca	gagaatggaa	120
agtcaaat	ccgtgaattg	tatgtgtctg	ggtttcatcc	atccgacatt	gaanttgact	180
tactgaagaa	tggnagagaa	attgaaaaag	tgagcattc	agacttgtct	ttcagcaagg	240
actggtcttt	ctatctctng	tactacactg	aattcacccc	cactgaaaaa	gatgagtatg	300
cctgccgtgt	gaaccatgtg	actttgtcac	agcccaagat	agtttaagtgg	gatcgagaca	360
tgtaagcagn	cnnatgggaa	gtttgaagat	gccgcatttg	gattggatga	attccaaatt	420
ctgcttgctt	gcntttta	antgatatgc	ntatacaccc	taccctttat	gncccaaat	480
tgtaggggtt	acatnantgt	tcnctnngga	catgatcttc	ctttataant	ccnccnttcg	540
aattgcccgt	cnccngttt	ngaattgttc	cnaaaccacg	gttggctccc	ccaggtcncc	600
tcttacggaa	gggcctgggc	cncctttncaa	ggttggggga	accnaaaatt	tcncttntgc	660
cncccncca	cnncttng	nnncanttt	ggaacccttc	cnattcccct	tggectcnna	720
nccttnncta	aaaaaacttn	aaancgtngc	naaanntttt	acttcccccc	ttacc	775

<210> 26  
 <211> 820  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(820)  
 <223> n = A,T,C or G

<400> 26						
anattantac	agtgtaatct	tttcccagag	gtgtgtanag	ggaacggggc	ctagaggcat	60
cccanagata	ncttatana	acagtgtctt	gaccaagagc	tgctgggcac	atttcctgca	120
gaaaagggtg	cggtcccat	cactcctcct	ctcccatagc	catcccagag	gggtgagtag	180
ccatcangcc	ttcggtggga	gggagtcang	gaaacaacan	accacagagc	anacagacca	240
ntgatgacca	tgggcgggag	cgagcctctt	ccctgnaccg	gggtggcana	nganagccta	300
nctgaggggt	cacactataa	acgttaacga	ccnagatnan	cacctgcttc	aagtgcaccc	360
ttcctacctg	acnaccang	accnnnaact	gcngcctggg	gacagcnctg	ggancagcta	420
acnnagcact	cacctgcccc	cccatggccg	tnccgntccc	tggtcctgnc	aagggaagct	480
ccctgttggg	attncgggga	naccaaggga	nccccctcct	ccanctgtga	aggaaaaann	540
gatggaat	ttcccttc	gccnntcccc	tcttcttcta	cacgccccct	nntactctc	600
tccctctntt	ntcctgnenc	acttttnacc	ccnnnatctc	ccttnattga	toggannctn	660

ganattccac tnnccctnc cntcnatcng naanacnaaa nactntctna cccnggggat 720  
 gggnnccctcg ntcatectct ctttttcnct accnccnntt ctttgctct ccttngatca  
 780tccaacntc gntggccntn ccccccnnn tcttttccc  
 820

<210> 27  
 <211> 818  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(818)  
 <223> n = A,T,C or G

<400> 27  
 tctgggtgat ggcctcttcc tcctcaggga cctctgactg ctctgggcca aagaatctct 60  
 tgtttcttct ccgagcccca ggcagcgggtg attcagccct gcccaacctg attctgatga 120  
 ctgctgatgc tgtgacggac ccaaggggca aatagggtcc cagggtccag ggaggggccc 180  
 ctgctgagca cttccgcccc tcacctgcc cagccctgc catgagctct gggctgggtc 240  
 tccgcctcca gggttctgct cttccangca ngccancaag tggcgtggg ccacactggc 300  
 ttcttctgc ccctccctg gctctganc tctgtctcc tgtctgtgc angcnccttg 360  
 gatctcagtt tcctcncctc anngaactct gttctgann tcttcantta actntgantt 420  
 tatnaccnan tggctgtnc tgtcnnactt taatgggccc gaccggetaa tccctccctc 480  
 nctcccttcc antcnnnna accngcttnc cntctctcc cntancccg ccngggaanc 540  
 ctcccttggc ctnaccangg gccnnnaccg cccntnctn ggggggcnng gtnnctnnc 600  
 ctgntncccc cnetcncnt tncctcgtcc cnnncnccn nngcannctc nengtcccn 660  
 tnnctctten ngntcgnaa ngntcncntn tnnnnngcn ngntnntn tccctctnc 720  
 cnnntgnang tnnntnnnc ncnngncccc nnnnnnnnn nggnntnnn tctnncnngc 780  
 cccnncccc ngnattaagg cctccnntct ccggccnc 818

<210> 28  
 <211> 731  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(731)  
 <223> n = A,T,C or G

<400> 28  
 aggaagggcg gagggatatt gtanggggatt gagggatagg agnataangg gggaggtgtg 60  
 tccaacatg anggtgnngt tctcttttga angaggggtg ngtttttann ccnggtgggt 120  
 gattnaaccc cattgtatgg agnnaaagg ttttagggat ttttcggctc ttatcagtat 180  
 ntanattcct gtnaatcgga aatnatntt tcnnccngaa aatnttgctc ccatccgnaa 240  
 attnctccc gtagtgcat nttngggggn cngccangtt tcccaggctg ctanaatcgt 300  
 actaaagntt naagtgggan tncaaatgaa aacctnncac agagnatccn taccgactg 360  
 tnnnttncct tcgcccctng actctgcnng agccaatac ccnngngnat gtcncccnng 420  
 nnnccgncnc tgaaannnnc tcngggctnn gancatcang gggtttcgca tcaaaagcnn 480  
 cgtttcncat naaggcaett tngcctcatc caaccnctng ccctcncca tttngccgtc 540  
 nggttcncct acgctnntng cncctnnntn ganattttnc ccgectnggg naancctcct 600  
 gnaatgggta gggnccttctc ttttnaccnn gnggtntact aatcnctnc acgcntnctt 660  
 tctcnacccc ccccttttt caatcccanc ggcnatagg gtctcccnng cgangggggg 720  
 nnnccannc c 731

<210> 29  
 <211> 822  
 <212> DNA  
 <213> Homo sapien

<220>

<221> misc\_feature  
 <222> (1)...(822)  
 <223> n = A,T,C or G

<400> 29

actagtccag	tgtggtggaa	ttccattgtg	ttggggncnc	ttctatgant	antnttagat	60
cgctcanacc	tcacancctc	ccnacnangc	ctataangaa	nannaataga	nctgtncnnt	120
atntntacnc	tcatanncct	cnnnaccac	tcctcttaa	ccctactgt	gcctatngcn	180
tnnctantct	ntgccgctn	cnanccaccn	gtgggcnac	cncnngnatt	ctcnatctcc	240
tcnccatntn	gcctananta	ngtncatacc	ctatacctac	nccaatgcta	nnnctaancn	300
tccatnantt	annntaacta	ccactgacnt	ngactttcnc	atnanctcct	aatttgaatc	360
tactctgact	cccacngcct	annnattagc	ancntcccc	nacnatntct	caaccaaadc	420
ntcaacaacc	tatctantcg	ttcnccaacc	nttncctccg	atccccnnac	aacccccctc	480
ccaaataccc	nccacctgac	ncctaaccn	caccatcccg	gcaagccnan	ggncatttan	540
ccactggaat	cacnatngga	naaaaaaac	ccnaactctc	tancncnnat	ctccctaana	600
aatnctcctn	naatttactn	ncantnccat	caancccaen	tgaaacnnaa	cccctgtttt	660
tanatccctt	ctttcgaaaa	ccnacccttt	annncccaac	ctttngggcc	ccccnctnc	720
ccnaatgaag	gncncccaat	cnangaaacg	ncntgaaaa	ancnaggcna	anannntccg	780
canatccctat	cccttanttn	ggggncctt	nccngggcc	cc		822

<210> 30  
 <211> 787  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(787)  
 <223> n = A,T,C or G

<400> 30

cggccgcctg	ctctggcaca	tgccctcctga	atggcatcaa	aagtgatgga	ctgcccattg	60
ctagagaaga	ccttctctcc	tactgtcatt	atggagccct	gcagactgag	ggctcccctt	120
gtctgcagga	tttgatgtct	gaagtcgtgg	agtgtggctt	ggagctcctc	atctacatna	180
gctggaagcc	ctggagggcc	tctctcgcca	gcctccccct	tctctccacg	ctctccangg	240
acaccagggg	ctccaggcag	cccattattc	ccagnangac	atggtgtttc	tccaagcgga	300
cccctggggc	ctgnaaggcc	agggctcctc	ttgaacacat	ctctcccgtc	ctgcctggca	360
ggcgtggga	tccactantt	ctanaacggg	cgccaccncg	gtgggagctc	cagcttttgt	420
tccnttaat	gaaggttaat	tgncgccttg	gcgtaatcat	nggtcanaac	tntttcctgt	480
gtgaaattgt	ttntccccctc	ncnattccnc	ncnacatacn	aaccgggaan	cataaagtgt	540
taaagcctgg	gggtngcctn	nngaataaac	tnaactcaat	taattgcgtt	ggctcatggc	600
ccgctttccn	ttcnggaaaa	ctgtcntccc	ctgcnttnnt	gaatcggcc	ccccccnggg	660
aaaagcggtt	tgcnttttng	gggntcctt	ccncttcccc	cctcnctaan	ccctnccct	720
cggtcgttnc	nggtngcggg	gaangggnat	nnnctcccnc	naagggggng	agnnnngtat	780
ccccaaa						787

<210> 31  
 <211> 799  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(799)  
 <223> n = A,T,C or G

<400> 31

tttttttttt	ttttttggc	gatgctactg	tttaattgca	ggaggtgggg	gtgtgtgtac	60
catgtaccag	ggctattaga	agcaagaagg	aaggagggag	ggcagagcgc	cctgctgagc	120
aacaaaggac	tcctgcagcc	ttctctgtct	gtctcttggc	gcaggcacat	ggggaggcct	180
cccgcagggt	gggggccacc	agtccagggg	tgggagcact	acanggggtg	ggagtgggtg	240
gtggctggtn	cnaatggcct	gncacanatc	cctacgattc	ttgacacctg	gatttcacca	300

ggggaccttc	tgttctccca	nggnaacttc	ntnmatctcn	aaagaacaca	actgtttctt	360
cngcanttct	ggctgttcat	ggaagcaca	ggtgtccnat	ttnggctggg	acttggtaca	420
tatggttcog	gcccacctct	ccntcnnaan	aagtaattca	ccccccccc	ccntctnttg	480
cctgggcctt	taantaccca	caccggaact	canttantta	ttcatcttng	gntgggcttg	540
ntnaticncn	cctgaangcg	ccaagttgaa	aggccacgcc	gtneccnctc	cccatagnan	600
nttttncnt	canctaatac	ccccccnggc	aacnatccaa	tccccccccc	tgggggcccc	660
agccccangc	ccccgnctcg	ggnnncngn	cncgnantcc	ccaggntctc	ccantcngnc	720
ccnnngcncc	cccgacgcga	gaacanaagg	ntngagccnc	cgcannnnnn	nggttnncac	780
ctcgcccccc	ccnnccgngg					799

<210> 32  
 <211> 789  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc feature  
 <222> (1)...(789)  
 <223> n = A,T,C or G

<400> 32						
tttttttttt	tttttttttt	tttttttttt	tttttttttt	tttttttttt	tttttttttt	60
tttttncnag	ggcaggttta	ttgacaacct	cncgggacac	aancaggctg	gggacaggac	120
ggcaacagcg	tccggcgggc	gcggcgggcg	ccctacctgc	ggtaccaaata	ntgcagcctc	180
cgctcccgc	tgatnttctt	ctgcagctgc	aggatgccnt	aaaacagggc	ctcgcccntn	240
ggtgggcacc	ctgggatttn	aatttccacg	ggcacaatgc	ggtcgcancc	cctcaccacc	300
nattaggaat	agtgtnttta	ccnccncccg	ttggcncact	ccccntggaa	accacttntc	360
gcggctccgg	catctgggtc	taaaccttgc	aaacnctggg	gccctctttt	tggttantnt	420
nccngccaca	atcatnactc	agactggcnc	gggtggcccc	caaaaaancn	ccccaaaacc	480
ggncatgtc	ttnnccgggt	tgctgcnatn	tncatcacct	cccgggcncn	ncaggncaac	540
ccaaaagtgc	ttgnggcccn	caaaaaanct	ccggggggnc	ccagtttcaa	caaagtcac	600
ccccttggcc	cccaaactct	ccccccgntt	ncgtgggttg	ggaacccacg	cctctnnctt	660
tggnnggcaa	gntgntccc	ccttcgggcc	cccgggtggc	ccnctcttaa	ngaaaaacnc	720
ntcctnnnca	ccatcccccc	nngnnacgnc	tancaangna	tccctttttt	tanaaacggg	780
ccccccnccg						789

<210> 33  
 <211> 793  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc feature  
 <222> (1)...(793)  
 <223> n = A,T,C or G

<400> 33						
gacagaacat	ggttgatggg	ggagcacctt	tctatacgac	ttacaggaca	gcagatgggg	60
aattcatggc	tggttgagca	atanaacccc	agttctacga	gctgctgac	aaaggacttg	120
gactaaaatc	tgatgaactt	cccaatcaga	tgagcatgga	tgattggcca	gaaatgaana	180
agaagtgtgc	agatgtattt	gcaaaagaaga	cgaaggcaga	gtggtgtcaa	atctttgacg	240
gcacagatgc	ctgtgtgact	ccggttctga	cttttgagga	ggttggtcat	catgatcaca	300
acaangaacg	gggctcggtt	atcaccantg	aggagcagga	cgtgagcccc	cgccctgcac	360
ctctgctggt	aaacacccca	gccatccctt	ctttcaaaaag	ggatccacta	cttctagagc	420
ggncgccacc	gcggtggagc	tccagctttt	gttcccttta	gtgagggtta	attgcgcgct	480
tggtcgtaac	atggtcatan	ctgtttcctg	tgtgaaattg	ttatccgctc	acaattccac	540
acaacatacg	anccggaagc	atnaaatttt	aaagcctggg	ggtngcctaa	tgantgaact	600
nactcacatt	aattggcttt	gcgctcactg	cccgttttcc	agtccggaaa	acctgtcctt	660
gccagctgcc	nttaatgaat	cnggccaccc	cccggggaaa	aggcngtttg	cttnttgggg	720
cgcnetcccc	gctttctcgc	ttcctgaant	ccttcccccc	ggtctttcgg	cttgccgcna	780
acggtatcna	cct					793

<210> 34  
 <211> 756  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(756)  
 <223> n = A,T,C or G

<400> 34  
 gccgcgaccg gcatgtacga gcaactcaag ggcgagtgg accgtaaaag ccccaatctt 60  
 ancaagtgcg gggaanagct gggtcgactc aagctagttc ttctggagct caacttcttg 120  
 ccaaccacag ggaccaagct gaccaaacag cagctaattc tggcccgta catactggag 180  
 atcggggccc aatggagcat cctacgcaan gacatcccct ccttcgagcg ctacatggcc 240  
 cagctcaaat gctactactt tgattacaan gagcagctcc ccgagtcagc ctatatgcac 300  
 cagctcttgg gcctcaacct cctcttctcg ctgtcccaga accgggtggc tgantnccac 360  
 acgganttgg ancggctgcc tgcccanga catacanacc aatgtctaca tcnaccacca 420  
 gtgtcctgga gcaatactga tgganggcag ctaccncaaa gtnttcttgg ccnagggtaa 480  
 catccccgcg cgagagctac accttcttca ttgacatcct gctcgacact atcagggatg 540  
 aaaatcgcn ggttgctcca gaaaggctnc aanaanatcc tttcnctga aggcccccg 600  
 atncnctagt nctagaatcg gcccgccatc gcggtgganc ctccaacctt tcgttnccct 660  
 ttactgaggg ttntattgcc cccttggcgt tatcatggc acnccngtn cctgtgttga 720  
 aattntaac ccccacaat tccacgcna catng 756

<210> 35  
 <211> 834  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(834)  
 <223> n = A,T,C or G

<400> 35  
 ggggatctct anatchacct gnatgcatgg ttgtcgggtg ggtcgctgtc gatgaanatg 60  
 aacaggatct tgcccttgaa gctctcggtc gctgtnttta agttgctcag tctgccgtca 120  
 tagtcagaca cncctcttgg caaaaaacan caggatntga gtcttgattt cacctccaat 180  
 aatcttcngg gctgtctgct cgggtgaactc gatgacnang ggcagctggg tgtgtntgat 240  
 aaantccanc angttctcct tggtagctc cccttcaaag ttgttcggc ctcatcaaa 300  
 cttctnnaan angannancc canctttgtc gagctggnat ttgganaaca cgctactgtt 360  
 ggaaactgat cccaaatggg atgtcatcca tcgcctctgc tgccctgcaa aaacttgctt 420  
 ggcncaaatc cgactcccn tccttgaaag aagccnatca caccctctc cctggactcc 480  
 nncaangact ctncgcctnc ccntccnng cagggttggg ggcannccgg gccntgcgc 540  
 ttcttcagcc agttcacnat ntcatcagc ccctctgcca gctgtntat tccttggggg 600  
 ggaanccgctc tctcccttcc tgaannaact ttgaccgtng gaatagccgc gcntcnccnt 660  
 acntnctggg ccgggttcaa antccctcn ttgcnntcn cctcgggcca ttctggattt 720  
 nccnaacttt ttcttcccc cncctcncgg ngtttggntt ttcatnngg ccccaactct 780  
 gctnttggcc antcccttgg gggcntntan cncctcctnt ggtccentng ggcc 834

<210> 36  
 <211> 814  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(814)  
 <223> n = A,T,C or G

<400> 36

cgngcgcgtt	ccngccgcgc	cccgtttcca	tgacnaaggc	tcccttcang	ttaaatacnn	60
cctagnaaac	attaatgggt	tgctctacta	atacatcata	cnaaccagta	agcctgcccc	120
naacgccaac	tcaggccatt	cctaccaaag	gaagaaaggc	tggtctctcc	accccctgta	180
ggaaaggcct	gccttgtaag	acaccacaat	ncggctgaat	ctnaagtctt	gtgttttact	240
aattggaaaa	aaaaataaac	aanaggtttt	gttctcatgg	ctgcccaccg	cagcctggca	300
ctaaaacanc	ccagcgctca	cttctgcttg	ganaaatatt	ctttgctctt	ttggacatca	360
ggcttgatgg	tatcactgcc	acntttccac	ccagctgggc	ncccttcccc	catntttgtc	420
antganctgg	aaggccctgaa	ncttagtctc	caaaagtctc	ngcccacaag	accggccacc	480
aggggagntc	ntttncagtg	gatctgccaa	anantaccn	tatcatcnnt	gaataaaaag	540
gcccctgaac	ganatgcttc	cancancctt	taagaccat	aatcctngaa	ccatgggtgcc	600
cttccggtct	gatecnaaag	gaatgttctt	gggtcccant	ccctcctttg	ttnccttacgt	660
tgtnttggac	cctngctngn	atnaccnaan	tganatcccc	ngaagcacc	tnccctggc	720
at ttganttt	cntaaattct	ctgccctacn	nctgaaagca	cnattccctn	ggcncnnaan	780
ggngaactca	agaaggtctn	ngaaaaacca	cncn			814

<210> 37  
 <211> 760  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(760)  
 <223> n = A,T,C or G

<400> 37						
gcatgctgct	cttccctcaaa	gttggttcttg	ttgccataac	aaccaccata	ggtaaagcgg	60
gcgcagtgtt	cgctgaagg	gtttagtac	cagcgcgga	tgctctcctt	gcagagtctt	120
gtgtctggca	ggccacgca	atgccctttg	tactgggga	aatggatgcg	ctggagctcg	180
tcaanccac	tcgtgtattt	ttcacangca	gcctcctccg	aagcntccgg	gcagtggggg	240
gtgtcgtcac	actccactaa	actgtcgatn	cancagccca	ttgctgcagc	ggaactgggt	300
gggtgacac	gtgccagaac	acactggatn	ggcctttcca	tggaaaggcc	tgggggaaat	360
cncctnancc	caaactgcct	ctcaaaggcc	accttgca	ccccgacagg	ctagaaatgc	420
actcttcttc	ccaaaggtag	ttgttcttgt	tgcccaagca	ncctccanca	aacccaaaanc	480
ttgcaaaatc	tgctccgtgg	gggtcatnnn	taccanggtt	ggggaaanaa	acccggcngn	540
ganccnccct	gtttgaatgc	naaggnaata	atcctcctgt	cttgcttggg	tggaaanagca	600
caattgaact	gttaacnttg	ggccnggttc	tctnggggtg	gtctgaaact	aatcaccgtc	660
actggaaaaa	ggtangtgcc	ttccttgaat	tcccaaantt	cccctngntt	tgggtntttt	720
ctcctctncc	ctaaaaatcg	tnttcccccc	ccntanggcg			760

<210> 38  
 <211> 724  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(724)  
 <223> n = A,T,C or G

<400> 38						
tttttttttt	tttttttttt	tttttttttt	tttttaaaaa	ccccctccat	tgaatgaaaa	60
cttccnaaat	tgccaacccc	cctcnnccaa	atnnccattt	ccgggggggg	gttccaaacc	120
caaattaatt	ttgganttta	aattaaatnt	tnattngggg	aanaanccaa	atgtnaagaa	180
aatttaaccc	attatnaact	taaatncctn	gaaacccntg	gnttccaaaa	atttttaacc	240
cttaaatccc	tccgaaattg	ntaanggaaa	accaaattcn	cctaaggctn	tttgaagggt	300
ngatttaaac	ccccttnant	tnttttnacc	cnngnctnaa	ntatttngnt	tccggtgttt	360
tccntttaan	cntnggtaac	tcccgntaat	gaannnccct	aanccaatta	aaccgaattt	420
tttttgaatt	ggaaattccn	ngggaattna	ccgggggttt	tcccntttgg	gggccatncc	480
ccncttttcg	gggtttgggn	ntaggttgaa	tttttnnang	ncccaaaaaa	ncccccaana	540
aaaaaactcc	caagnnttaa	ttngaattnc	ccccctccca	ggccttttgg	gaaagngggg	600
ttnttggggg	ccngggantt	cnttcccccn	ttncncccc	ccccccnggt	aaanggttat	660

ngnnttttgggt ttttggggccc cttnanggac cttccggatn gaaattaaat ccccgggncg 720  
gccc 724

<210> 39  
<211> 751  
<212> DNA  
<213> Homo sapien  
  
<220>  
<221> misc\_feature  
<222> (1)...(751)  
<223> n = A,T,C or G

<400> 39  
tttttttttt tttttctttg ctcacattta atttttattt tgattttttt taatgctgca 60  
caacacaata tttatttcat ttgtttcttt tatttcattt tatttgtttg ctgctgctgt 120  
tttatttatt tttactgaaa gtgagaggga actttttgtg ccttttttcc tttttctgta 180  
ggccgcctta agcttttctaa atttggaaaca tctaagcaag ctgaanggaa aaggggggtt 240  
cgcaaaatca ctccgggggaa nggaaagggt gctttgttaa tcatgcccta tgggtgggtga 300  
ttaactgctt gtacaattac ntttcacttt taattaattg tgctnaangc ttttaattana 360  
cttggggggt ccctccccc accaaccctt .ctgacaaaaa gtgccngccc tcaaatnatg 420  
tccccgcntt cnttgaaaca cacngcngaa ngttctcatt ntcccccnc caggtnaaaa 480  
tgaaagggtta ccatntttta cncacactcc acntggcnnn gcctgaatcc tcnaaaancn 540  
ccctcaancn aattnctnng cccccgtcnc gcntnngtcc cccccgggt cggggaantr 600  
caccccnnga anncnntnnc naacnaaatt ccgaaaatat tcccnntcnc tcaattcccc 660  
cnnagactnt cctcnncnan cncaattttc tttntntcac gaacncgnnc cnnaaaatgn 720  
nnnncnctc cncnngtcen naatcnccan c 751

<210> 40  
<211> 753  
<212> DNA  
<213> Homo sapien  
  
<220>  
<221> misc\_feature  
<222> (1)...(753)  
<223> n = A,T,C or G

<400> 40  
gtggtatttt ctgtaagatc aggtgttcct ccctcgtagg tttagaggaa acaccctcat 60  
agatgaaaac ccccccgaga cagcagcact gcaactgcca agcagccggg gtaggagggg 120  
cgccctatgc acagctgggc ccttgagaca gcagggttc gatgtcaggc tcgatgtcaa 180  
tggtctggaa gcggcggtg tactgctgta ggggcacacc gtcagggcc accaggaact 240  
tctcaaagtt ccaggcaacn tcgttgcgac acaccggaga ccagggtgatn agcttgggggt 300  
cggtcataan cgcggtggcg tcgtcgctgg gagctggcag ggcctcccgc aggaaggcna 360  
ataaaagggt cgcccccgca ccgttcantc cgcacttctc naanaccatg angttgggct 420  
cnaaccaccc accannccgg acttccttga nggaattccc aaatctcttc gntcttgggc 480  
ttctnctgat gccctanctg gttgccnngn atgccaanca nccccaancc ccggggtcct 540  
aaanacccn cctcctcntt tcatctgggt tnttntcccc ggaccntggt tcctctcaag 600  
ggancccata tctcnaccan tactcaccnt nccccccnt gnnaccanc cttctanngn 660  
ttccnccccg ncctctggcc cntcaaanan gcttnacna cctgggtctg ccttcccccc 720  
tnccctatct gnaccccn cn tttgtctcan tnt 753

<210> 41  
<211> 341  
<212> DNA  
<213> Homo sapien

<400> 41  
actatatcca tcacaacaga catgcttcat cccatagact tcttgacata gcttcaaagt 60  
agtgaacca tccttgattt atatacatat atgttctcag tattttggga gcctttccac 120  
ttctttaaac cttgttcatt atgaacactg aaaataggaa tttgtgaaga gttaaaaagt 180

tatagcttgt ttacgtagta agtttttgaa gtctacattc aatccagaca cttagttgag	240
tgttaaactg tgatttttaa aaaatatcat ttgagaatat tctttcagag gtattttcat	300
ttttactttt tgattaattg tgttttatat attagggtag t	341

<210> 42  
<211> 101  
<212> DNA  
<213> Homo sapien

<400> 42	
acttactgaa tttagttctg tgctcttcct tatttagtgt tgtatcataa atactttgat	60
gtttcaaaca ttctaaataa ataattttca gtggcttcac a	101

<210> 43  
<211> 305  
<212> DNA  
<213> Homo sapien

<400> 43	
acatctttgt tacagtctaa gatgtgttct taaatcacca ttccttcctg gtcctcacc	60
tccagggtgg tctcacactg taattagagc tattgaggag tctttacagc aaattaagat	120
tcagatgcct tgctaagtct agagttctag agttatgttt cagaaagtct aagaaaccca	180
cctcttgaga ggtcagtaaa gaggacttaa tatttcatat ctacaaaatg accacaggat	240
tggtacacaga acgagagtta tcttggtataa ctacagagctg agtacctgcc cgggggcccgc	300
tcgaa	305

<210> 44  
<211> 852  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc feature  
<222> (1)... (852)  
<223> n = A,T,C or G

<400> 44	
acataaatat cagagaaaag tagtctttga aatatttacg tccaggagtt ctttgtttct	60
gattatttgg tgtgtgtttt ggtttgtgtc caaagtattg gcagcttcag ttttcatttt	120
ctctccatcc tcgggcattc ttcccaaatt tatataccag tcttcgtcca tccacacgct	180
ccagaatttc tctttttag tagtatctca tagctcggct gagcttttca taggtcatgc	240
tgctgttgtt ctctttttta ccccatagct gagccactgc ctctgatttc aagaacctga	300
agacgccttc agatcggctc tccattttta ttaatcctgg gttcttgtct ggggtcaaga	360
ggatgtcgcg gatgaattcc cataagttag tccctctcgg gttgtgcttt ttgggtgtggc	420
acttgccagg ggggtcttgc tcctttttca tatcaggtga ctctgcaaca ggaaggtgac	480
tggtggttgt catggagatc tgagcccggc agaaagtgtt gctgtccaac aaatctactg	540
tgctaccata gttggtgtca tataaatagt tctngtcttt ccagggtgtc atgatggaag	600
gctcagtttg ttcagtcttg acaatgacat tgtgtgtgga ctggaacagg tcactactgc	660
actggccgtt ccacttcaga tgctgcaagt tgctgtagag gagntgcccc gccgtccctg	720
ccgcccgggt gaactcctgc aaactcatgc tgcaaagggt ctgccggttg atgtcgaact	780
cntggaagg gatacaattg gcatccagct ggttgggtgc caggaggtga tggagccact	840
cccacacctg gt	852

<210> 45  
<211> 234  
<212> DNA  
<213> Homo sapien

<400> 45	
acaacagacc cttgctcgtc aacgacctca tgctcatcaa gttggacgaa tccgtgtccg	60
agtctgacac catccggagc atcagcattg ctctgcagtg ccctaccgcg gggaaactctt	120
gcctcgtttc tggtgtgggt ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg	180



tgaacgtgtc ggtggtgtct gaggaggtct gcagtaagct ctatgacccg ctgt

234

<210> 46  
 <211> 590  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(590)  
 <223> n = A,T,C or G

<400> 46  
 acttttttatt taaatgttta taaggcagat ctatgagaat gatagaaaac atggtgtgta 60  
 atttgatagc aatatttttg agattacaga gtttttagtaa ttaccaatta cacagttaaa 120  
 aagaagataa tatattccaa gcanatacaa aatatctaata gaaagatcaa ggcaggaaaa 180  
 tgantataac taattgacaa tggaaaatca attttaatgt gaattgcaca ttatccttta 240  
 aaagctttca aaanaaanaa ttattgcagt ctanttaatt caaacagtgt taaatggtat 300  
 caggataaan aactgaaggg canaaagaat taattttcac ttcattgtaac ncacccanatt 360  
 ttacaatggc ttaaatgcan ggaaaaagca gtggaagtag ggaagtantc aaggtccttc 420  
 tggctctctaa tctgccttac tctttgggtg tggctttgat cctctggaga cagctgccag 480  
 ggctcctgtt atatccacaa tcccagcagc aagatgaagg gatgaaaaag gacacatgct 540  
 gccttccttt gaggagactt catctcactg gccaacactc agtcacatgt 590

<210> 47  
 <211> 774  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(774)  
 <223> n = A,T,C or G

<400> 47  
 acaagggggc ataatagaagg agtgggggana gatttttaaag aaggaaaaaa aacgaggccc 60  
 tgaacagaat ttctcctgnac aacgggggctt caaaataatt ttcttgggga ggttcaagac 120  
 gcttcactgc ttgaaactta aatggatgtg ggacanaatt ttctgtaatg accctgaggg 180  
 cattacagac gggactctgg gaggaaggat aaacagaaaag gggacaaaag ctaatcccaa 240  
 aacatcaaag aaaggaagggt ggcgtcatat cccccagcct acacagttct ccagggtctt 300  
 cctcatccct ggaggacgac agtggaggaa caactgacca tgtccccagg ctctgtgtg 360  
 ctggctcctg gtcttcagcc cccagctctg gaagcccacc ctctgctgat cctgcgtggc 420  
 ccacactcct tgaacacaca tcccaggtt atattcctgg acatggctga acctcctatt 480  
 cctacttccg agatgccttg ctccctgcag cctgtcaaaa tcccactcac cctccaaacc 540  
 acggcatggg aagcctttct gacttgcttg attactccag catcttggaa caatccctga 600  
 ttccccactc cttagaggca agataggggtg gtttaagagta gggctggacc acttggagcc 660  
 aggtgctggt cttcaaattt tggctcattt acgagctatg ggaccttggg caagtnatct 720  
 tcacttctat gggcntcatt ttgttctacc tgcaaaatgg gggataataa tagt 774

<210> 48  
 <211> 124  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(124)  
 <223> n = A,T,C or G

<400> 48  
 canaaaattga aattttataa aaaggcattt ttctcttata tccataaaat gatataattt 60  
 ttgcaantat anaaatgtgt cataaattat aatgttcctt aattacagct caacgcaact 120

tggt

124

<210> 49  
 <211> 147  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(147)  
 <223> n = A,T,C or G

<400> 49  
 gccgatgcta ctatttttatt gcaggagggtg ggggtgtttt tattattctc tcaacagctt 60  
 tgtggctaca ggtggtgtct gactgcatna aaaanttttt tacgggtgat tgcaaaaatt 120  
 ttagggcacc catatcccaa gcantgt 147

<210> 50  
 <211> 107  
 <212> DNA  
 <213> Homo sapien

<400> 50  
 acattaaatt aataaaagga ctgttgggggt tctgctaaaa cacatggctt gatattattgc 60  
 atggtttgag gttaggagga gttaggcata tgttttggga gaggggt 107

<210> 51  
 <211> 204  
 <212> DNA  
 <213> Homo sapien

<400> 51  
 gtcctaggaa gtctagggga cacacgactc tggggtcacg gggccgacac acttgacggt 60  
 cgggaaggaa aggcagagaa gtgacaccgt cagggggaaa tgacagaaag gaaaatcaag 120  
 gccttgcaag gtcagaaagg ggactcaggg cttccaccac agccctgccc cacttgcca 180  
 cctccctttt gggaccagca atgt 204

<210> 52  
 <211> 491  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(491)  
 <223> n = A,T,C or G

<400> 52  
 acaaagataa catttatctt ataacaaaaa tttgatagtt tttaaagggtta gtattgtgta 60  
 ggggtattttc caaaagacta aagagataac tcaggtaaaa agttagaaat gtataaaaca 120  
 ccatcagaca ggttttttaa aaacaacata ttacaaaatt agacaatcat ccttaaaaaa 180  
 aaaactttct gtatcaattt cttttgttca aaatgactga cttaantatt tttaaatatt 240  
 tcanaaacac ttcctcaaaa attttcaana tggtagcttt canatgtnc ctcagtcca 300  
 atgttgctca gataaataaa tctcgtgaga acttaccacc caccacaagc tttctggggc 360  
 atgcaacagt gtcctttctt tnccttttct ttttttttt ttacaggcac agaaactcat 420  
 caattttatt tggataacaa aggggtctcca aattatattg aaaaataaat ccaagttaat 480  
 atcactcttg t 491

<210> 53  
 <211> 484  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(484)  
 <223> n = A,T,C or G

<400> 53  
 acataattta gcagggctaa ttaccataag atgctattta ttaanaggtn tatgatctga 60  
 gtattaacag ttgctgaagt ttggtatttt tatgcagcat tttctttttg ctttgataac 120  
 actacagaac ccttaaggac actgaaaatt agtaagtaaa gttcagaaac attagctgct 180  
 caatcaaadc tctacataac actatagtaa ttaaaacggt aaaaaaaagt gttgaaatct 240  
 gcactagtat anaccgctcc tgtcaggata anactgcttt ggaacagaaa gggaaaaanc 300  
 agcttttgant ttctttgtgc tgatangagg aaaggctgaa ttaccttggt gcctctccct 360  
 aatgattggc aggtcnggta aatnccaaaa catattccaa ctcaacactt cttttccncg 420  
 tanccttgant ctgtgtattc caggancagg cggatggaat gggccagccc ncggatgttc 480  
 cant 484

<210> 54  
 <211> 151  
 <212> DNA  
 <213> Homo sapien

<400> 54  
 actaaacctc gtgcttggtga actccataca gaaaacggtg ccatccctga acacggctgg 60  
 ccactgggta tactgctgac aaccgcaaca acaaaaacac aaatccttgg cactggctag 120  
 tctatgtcct ctcaagtgcc tttttgtttg t 151

<210> 55  
 <211> 91  
 <212> DNA  
 <213> Homo sapien

<400> 55  
 accctggcttg tctccgggtg gttcccggcg cccccacgg tccccagaac ggacactttc 60  
 gccctccagt ggatactcga gccaaagtgg t 91

<210> 56  
 <211> 133  
 <212> DNA  
 <213> Homo sapien

<400> 56  
 ggcggatgtg cggttggttat atacaaatat gtcattttat gtaagggact tgagtatact 60  
 tggatttttg gtatctgtgg gttgggggga cggctccagga accaataccc catggatacc 120  
 aagggacaac tgt 133

<210> 57  
 <211> 147  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(147)  
 <223> n = A,T,C or G

<400> 57  
 actctggaga acctgagccg ctgctccgcc tctgggatga ggtgatgcac gcngtggcgc 60  
 gactgggagc tgagcccttc cctttgcgcc tgccctcagag gattgttgcc gacntgcana 120  
 tctcantggg ctggatncat gcagggt 147

<210> 58

<211> 198  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc feature  
 <222> (1)...(198)  
 <223> n = A,T,C or G

<400> 58  
 acagggatat aggtttnaag ttattgtnat tgtaaaatac attgaatttt ctgtatactc 60  
 tgattacata catttatcct ttaaaaaaga tgtaaatcct aatttttatg ccatctatta 120  
 atttaccat gagttacctt gtaaatgaga agtcatgata gcactgaatt ttaactagtt 180  
 ttgacttcta agtttggt 198

<210> 59  
 <211> 330  
 <212> DNA  
 <213> Homo sapien

<400> 59  
 acaacaaatg ggttgtagg aagtcttctc agcaaaactg gtgatggcta ctgaaaagat 60  
 ccattgaaaa ttatcattaa tgatttttaa tgacaagtta tcaaaaactc actcaatttt 120  
 cacctgtgct agcttgctaa aatgggagtt aactctagag caaatatagt atcttctgaa 180  
 tacagtcaat aaatgacaaa gccagggcct acaggtggtt tccagacttt ccagaccag 240  
 cagaaggaat ctattttatc acatggatct ccgtctgtgc tcaaaatacc taatgatatt 300  
 tttcgtcttt attggacttc tttgaagagt 330

<210> 60  
 <211> 175  
 <212> DNA  
 <213> Homo sapien

<400> 60  
 accgtgggtg ctttctacat tcctgacggc tccttcacca acatctggtt ctacttcggc 60  
 gtcgtgggct ctttctctt catcctcatc cagctgggtc tgctcatcga ctttgcgcac 120  
 tcctggaacc agcgggtggc gggcaaggcc gaggagtgcg attcccgtgc ctggt 175

<210> 61  
 <211> 154  
 <212> DNA  
 <213> Homo sapien

<400> 61  
 accccacttt tcctcctgtg agcagtctgg acttctcact gctacatgat gagggtgagt 60  
 ggtgtgtgct cttcaacagt atcctcccct ttccggatct gctgagccgg acagcagtgc 120  
 tggactgcac agccccggg ctccacattg ctgt 154

<210> 62  
 <211> 30  
 <212> DNA  
 <213> Homo sapien

<400> 62  
 cgctcgagcc ctatagttag tcgtattaga 30

<210> 63  
 <211> 89  
 <212> DNA  
 <213> Homo sapien

<400> 63

acaagtcatt tcagcaccct ttgctcttca aaactgacca tcttttatat ttaatgcttc 60  
ctgtatgaat aaaaatggtt atgtcaagt 89

<210> 64  
<211> 97  
<212> DNA  
<213> Homo sapien

<400> 64  
accggagtaa ctgagtcggg acgctgaatc tgaatccacc aataaataaa ggttctgcag 60  
aatcagtga tccaggattg gtccttgat ctggggt 97

<210> 65  
<211> 377  
<212> DNA  
<213> Homo sapien  
  
<220>  
<221> misc feature  
<222> (1)...(377)  
<223> n = A,T,C or G

<400> 65  
acaacaanaa ntcccttctt taggcactg atggaaacct ggaaccccct tttgatggca 60  
gcatggcgct ctaggccttg acacagcggc tggggtttgg gctntcccaa accgcacacc 120  
ccaaccctgg tctaccaca nttctggcta tgggctgtct ctgccactga acatcaggggt 180  
tcggtcataa natgaaatcc caanggggac agaggtcagt agaggaaagct caatgagaaa 240  
ggtgctgttt gctcagccag aaaacagctg cctggcattc gccgctgaac tatgaaccg 300  
tgggggtgaa ctacccccc gaggaatcat gcctgggcga tgcaanggtg ccaacaggag 360  
ggcggggagg agcatgt 377

<210> 66  
<211> 305  
<212> DNA  
<213> Homo sapien

<400> 66  
acgcctttcc ctcagaattc agggaagaga ctgtcgctg ccttcctccg ttgttgctg 60  
agaaccctg tgcccttcc caccatatcc accctcgctc catctttgaa ctcaaacacg 120  
aggaaactaac tgcacctgg tctctctccc agtccccagt tcacctcca tccctcacct 180  
tcctccactc taagggatat caacactgcc cagcacaggg gccctgaatt tatgtggtt 240  
ttatatattt ttaataaga tgcactttat gtcatttttt aataaagtct gaagaattac 300  
tgttt 305

<210> 67  
<211> 385  
<212> DNA  
<213> Homo sapien

<400> 67  
actacacaca ctccacttgc ctttgtgaga cactttgtcc cagcacttta ggaatgctga 60  
ggtcggacca gccacatctc atgtgcaaga ttgccagca gacatcaggt ctgagagttc 120  
cccttttaaa aaaggggact tgcttaaaaa agaagtctag ccacgattgt gtagagcagc 180  
tgtgctgtgc tggagattca cttttgagag agttctctc tgagacctga tctttagagg 240  
ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgcttg 300  
cctctcccag ggccccagcc tggccacacc tgcttacagg gcactctcag atgccatac 360  
catagtttct gtgctagtgg accgt 385

<210> 68  
<211> 73  
<212> DNA  
<213> Homo sapien

<400> 68  
 acttaaccag atatattttt accccagatg gggatattct ttgtaaaaaa tgaaaataaa 60  
 gtttttttaa tgg 73

<210> 69  
 <211> 536  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(536)  
 <223> n = A,T,C or G

<400> 69  
 actagtccag tgtggtggaa ttccattgtg ttgggggctc tcacctcct ctctgcagc 60  
 tccagctttg tgctctgcct ctgaggagac catggcccag catctgagta cctgtctgct 120  
 cctgctggcc accctagctg tggccctggc ctggagcccc aaggaggagg ataggataat 180  
 cccgggtggc atctataacg cagacctcaa tgatgagtgg gtacagcgtg cccttcactt 240  
 cgccatcagc gagtataaca aggccaccaa agatgactac tacagacgtc cgctgcgggt 300  
 actaagagcc aggaacacaga ccgttggggg ggtgaattac ttcttcgacg tagaggtggg 360  
 ccgaaccata tgtaccaagt cccagcccaa cttggacacc tgtgccttcc atgaacagcc 420  
 agaactgcag aagaaacagt tgtgctcttt cgagatctac gaagttccct ggggagaaca 480  
 gaangtcctt ggtgaaatc caggtgtcaa gaaatcctan ggatctgttg ccaggc 536

<210> 70  
 <211> 477  
 <212> DNA  
 <213> Homo sapien

<400> 70  
 atgacccta acagggggcc tctcagccct cctaattgacc tccggcctag ccatgtgatt 60  
 tcacttccac tccataacgc tcctcatact aggcctacta accaacacac taaccatata 120  
 ccaatgatgg cgcgatgtaa cagagaaaag cacataccaa ggccaccaca caccacctgt 180  
 ccaaaaaggc cttcgatacg ggataatcct atttattacc tcagaagttt ttttcttcgc 240  
 agggattttt ctgagccttt taccactoca gcctagcccc taccocccaa ctaggagggc 300  
 actggccccc aacaggcatc accccgctaa atcccctaga agtcccactc ctaaacacat 360  
 ccgtattact cgcacagga gtatcaatca cctgagctca ccatagtcta atagaaaaca 420  
 accgaaacca aattattcaa agcactgctt attacaattt tactgggtct ctatttt 477

<210> 71  
 <211> 533  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(533)  
 <223> n = A,T,C or G

<400> 71  
 agagctatag gtacagtgtg atctcagctt tgcaaacaca ttttctacat agatagtact 60  
 aggtattaat agatatgtaa agaaagaaat cacaccatta ataattgtaa gattggttta 120  
 tgtgatttta gtggtatttt tggcaccctt atatattgtt tccaaacttt cagcagtgat 180  
 attatttcca taacttaaaa agtgagtttg aaaaagaaaa tctccagcaa gcatctcatt 240  
 taaataaagg tttgtcatct ttaaaaatac agcaatatgt gactttttta aaaagctgtc 300  
 aaataggtgt gaccctacta ataattatta gaaatacatt taaaaacatc gagtacctca 360  
 agtcagtttg ccttgaaaaa tatcaaatat aactcttaga gaaatgtaca taaaagaatg 420  
 cttcgttaatt ttggagtang aggttccttc ctcaattttg tattttttaa aagtacatgg 480  
 taaaaaaaaa aattcacaac agtatataag gctgtaaaat gaagaattct gcc 533

<210> 72

<211> 511  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (511)  
 <223> n = A,T,C or G

<400> 72  
 tattacggaa aaacacacca cataattcaa ctancaaaga anactgcttc agggcggtga 60  
 aatgaaagg cttccaggca gttatctgat taaagaacac taaaagaggg acaaggctaa 120  
 aagccgcagg atgtctacac tatancaggc gctatttggg ttggctggag gagctgtgga 180  
 aaacatggan agattgggtgc tgganatcgc cgtggctatt cctcattgtt attacanagt 240  
 gaggttctct gtgtgccac tggtttgaaa accgttctnc aataatgata gaatagtaca 300  
 cacatgagaa ctgaaatggc ccaaaccag aaagaaagcc caactagatc ctcagaanac 360  
 gcttctaggg acaataaccg atgaagaaaa gatggcctcc ttgtgcccc gtctgttatg 420  
 atttctctcc attgcagcna naaaccggt cttctaagca aacncagggt atgatggcna 480  
 aaatacacc cctcttgaag naccnggagg a 511

<210> 73  
 <211> 499  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (499)  
 <223> n = A,T,C or G

<400> 73  
 cagtgcagc actggtgccg gtaccagtag caataacagt gccagtgccg gtgccagcac 60  
 cagtgggtggc ttcagtgtctg gtgccagcct gaccgccact ctcacatttg ggctcttcgc 120  
 tggccttggg ggagctgggt ccagcaccag tggcagctct ggtgcctgtg gtttctccta 180  
 caagttagat ttttagatatt gttaatctct ccagctcttc tcttcaagcc aggggtgcac 240  
 ctgagaaacc tactcaacac agcactctag gcagccacta tcaatcaatt gaagttagaca 300  
 ctctgcatta aatctatttg ccatttctga aaaaaaaaaa aaaaaaaggg cggccgctcg 360  
 antcttaggg gccggtttaa acccgctgat cagcctcgac tgtgccttct anttgccagc 420  
 catctgttgt ttgcccctcc cccgntgcct tccttgacct tggaaagtgc cactcccact 480  
 gtcctttcct aantaaaat 499

<210> 74  
 <211> 537  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)... (537)  
 <223> n = A,T,C or G

<400> 74  
 tttcatagga gaacacactg aggagatact tgaagaattt ggattcagcc gcgaagagat 60  
 ttatcagctt aactcagata aaatcattga aagtaataag gtaaaagcta gtctctaact 120  
 tccaggccca cggctcaagt gaatttgaat actgcattta cagtgtagag taacacataa 180  
 cattgtatgc atggaaacat ggaggaacag tattacagtg tcctaccact ctaatcaaga 240  
 aaagaattac agactctgat tctacagtga tgattgaatt ctaaaaatgg taatcattag 300  
 ggcttttgat ttataanact ttgggtactt atactaaatt atggtagtta tactgccttc 360  
 cagtttgctt gatataattg ttgatattaa gattcttgac ttatattttg aatgggttct 420  
 actgaaaaan gaatgatata ttcttgaaga catcgatata catttattta cactcttgat 480  
 tctacaatgt agaaaatgaa ggaaatgcc caaattgtat ggtgataaaa gtcccgt 537

<210> 75  
 <211> 467  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(467)  
 <223> n = A,T,C or G

<400> 75  
 caaanacaat tgttcaaaag atgcaaatga tacactactg ctgcagctca caaacacctc 60  
 tgcataattac acgtacctcc tcctgctcct caagtagtgt ggtctatatt gccatcatca 120  
 cctgctgtct gcttagaaga acggctttct gctgcaangg agagaaatca taacagacgg 180  
 tggcacaagg aggccatctt ttctcatcgt gttattgtcc ctagaagcgt cttctgagga 240  
 tctagtggg ctttctttct gggtttgggc catttcantt ctcattgtgt tactattcta 300  
 tcattattgt ataacgggtt tcaaaccngt gggcacncag agaaccctcac tctgtaataa 360  
 caatgaggaa tagccacggg gatctccagc accaaatctc tccatgttnt tccagagctc 420  
 ctccagccaa cccaaatagc cgctgctatn gtgtagaaca tccctgn 467

<210> 76  
 <211> 400  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(400)  
 <223> n = A,T,C or G

<400> 76  
 aagctgacag cattcggggc gagatgtctc gctccgtggc cttagctgtg ctgcgctac 60  
 tctctctttc tggcctggag gctatccagc gtactccaaa gattcagggt tactcacgtc 120  
 atccagcaga gaatggaaaag tcaaatttcc tgaattgcta tgtgtctggg ttcatccat 180  
 ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaagt gagcattcag 240  
 acttgtcttt cagcaaggac tggcttttct atctcttgta ctacactgaa ttcaccccca 300  
 ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng 360  
 ttnagtggga tcganacatg taagcagcan catgggaggt 400

<210> 77  
 <211> 248  
 <212> DNA  
 <213> Homo sapien

<400> 77  
 ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct 60  
 ccagctgccc cggcggggga tgcgaggtcc ggagcacctc tgcccggctg tgattgtctc 120  
 caggcactgt tcatctcagc ttttctgtcc ctttgtctcc ggcaagcgt tctgctgaaa 180  
 gttcatatct ggagcctgat gtcttaacga ataaaggtcc catgctccac ccgaaaaaaa 240  
 aaaaaaaa 248

<210> 78  
 <211> 201  
 <212> DNA  
 <213> Homo sapien

<400> 78  
 actagtccag tgtggtggaa ttccattgtg ttgggcccaa cacaatggct acctttaaca 60  
 tcaccagac cccgccctgc ccgtgcccc cgtgctgtc aacgacagta tgatgcttac 120  
 tctgtactc ggaaactatt tttatgtaat taatgtatgc tttcttgttt ataaatgcct 180  
 gatttaaaaa aaaaaaaaaa a 201



<210> 79  
 <211> 552  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(552)  
 <223> n = A,T,C or G

<400> 79  
 tccttttgtt aggtttttga gacaacccta gacctaaact gtgtcacaga cttctgaatg 60  
 tttaggcagt gctagtaatt tcctcgtaat gattctgtta ttactttcct attctttatt 120  
 cctctttctt ctgaagatta atgaagttga aaattgaggt ggataaatac aaaaaggtag 180  
 tgtgatagta taagtatcta agtgcagatg aaagtgtgtt atatatatcc attcaaaatt 240  
 atgcaagtta gtaattactc aggggttaact aaattacttt aatatgctgt tgaacctact 300  
 ctgttccttg gctagaaaaa attataaaaca ggactttgtt agtttgggaa gccaaattga 360  
 taatattcta tgttctaataa gttgggctat acataaanta tnaagaaata tggaatttta 420  
 ttcccaggaa tatgggggttc atttatgaat antaccggg anagaagttt tgantnaaac 480  
 cngttttggt taatacgtta atatgtcctn aatnaacaag gcntgactta tttccaaaaa 540  
 aaaaaaaaaa aa 552

<210> 80  
 <211> 476  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(476)  
 <223> n = A,T,C or G

<400> 80  
 acagggattt gagatgctaa ggccccagag atcgtttgat ccaaccctct tattttcaga 60  
 ggggaaaatg gggcctagaa gttacagagc atctagctgg tgcgctggca cccctggcct 120  
 cacacagact cccgagtagc tgggactaca ggcacacagt cactgaagca ggccctgttt 180  
 gcaattcacg ttgccacctc caacttaaac attcttcata tgtgatgtcc ttagtcacta 240  
 aggttaaaact ttcccaccca gaaaaggcaa cttagataaa atcttagagt actttcatac 300  
 tcttctaagt cctcttccag cctcactttg agtcctcctt gggggttgat aggaantntc 360  
 tcttggttt ctcaataaaa tctctatcca tctcatgtt aatttggtac gcntaaaaat 420  
 gctgaaaaaa ttaaaatgtt ctgggtttcnc tttaaaaaaa aaaaaaaaaa aaaaaa 476

<210> 81  
 <211> 232  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(232)  
 <223> n = A,T,C or G

<400> 81  
 tttttttttg tatgcentcn ctgtggngtt attgttgctg ccaccctgga ggagcccagt 60  
 ttcttctgta tctttctttt ctgggggagc ttcttggtc tggccctcca ttcccagcct 120  
 ctcatcccca tcttgcaactt ttgctagggt tggaggcgct ttcttggttag cccctcagag 180  
 actcagtcag cgggaataag tcctaggggt ggggggtgtg gcaagccggc ct 232

<210> 82  
 <211> 383  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(383)  
 <223> n = A,T,C or G

<400> 82  
 aggcgggagc agaagctaaa gccaaagccc aagaagagtgc cagtgccag cactgggtgcc 60  
 agtaccagta ccaataacat gccagtgccag gtgccagcac cagtgggtggc ttcagtgtgtg 120  
 gtgccagcct gaccgccact ctcacatttg ggctcttcgc tggccttggg ggagctgggtg 180  
 ccagcaccag tggcagctct ggtgcctgtg gtttctccta caagtgagat tttagatatt 240  
 gttaatcctg ccagtctttc tcttcaagcc aggggtgcac ctcagaaacc tactcaacac 300  
 agcactctng gcagccacta tcaatcaatt gaagttgaca ctctgcatta aatctatttg 360  
 ccatttcaaa aaaaaaaaaa aaa 383

<210> 83  
 <211> 494  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(494)  
 <223> n = A,T,C or G

<400> 83  
 accgaattgg gaccgctggc ttataagcga tcatgtcctc cagtattacc tcaacgagca 60  
 gggagatcga gtctatacgc tgaagaaatt tgacccgatg ggacaacaga cctgtctcagc 120  
 ccatcctgct cgggtctccc cagatgacaa atactctcga caccgaatca ccatcaagaa 180  
 acgcttcaag gtgctcatga ccagcaacc gcgccctgtc ctctgagggg ccttaaaactg 240  
 atgtcttttc tgccacctgt taccctctcg agactccgta accaaactct tcggactgtg 300  
 agccctgatg cctttttgcc agccatactc ttggcntcc agtctctcgt ggcgattgat 360  
 tatgcttggtg tgaggcaatc atggtggcat caccatnaa gggaacacat ttgantttt 420  
 tttcncatat tttaaattac naccagaata nttcagaata aatgaattga aaaactctta 480  
 aaaaaaaaaa aaaa 494

<210> 84  
 <211> 380  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(380)  
 <223> n = A,T,C or G

<400> 84  
 gctggtagcc tatggcgtgg ccacgggangg gctcctgagg cacgggacag tgacttccca 60  
 agtatcctgc gccgcgtctt ctaccgtccc tacctgcaga tcttcgggca gattcccccag 120  
 gaggacatgg acgtggccct catggagcac agcaactgct cgctggagcc cggcttctgg 180  
 gcacaccctc ctggggccca ggcgggcacc tgcgtctccc agtatgccaa ctggctgggtg 240  
 gtgtgctcc tcgtcatctt cctgctcgtg gccaacatcc tgctgggtcac ttgctcattg 300  
 ccatgttcag ttacacattc ggcaaagtac agggcaacag cnatctctac tgggaaggcc 360  
 agcgttnccg cctcatccgg 380

<210> 85  
 <211> 481  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature

&lt;222&gt; (1)...(481)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 85

gagtttagctc	ctccacaacc	ttgatgaggt	cgtctgcagt	ggcctctcgc	ttcataccgc	60
tnccatcgctc	atactgtagg	tttgccacca	cctcctgcat	cttggggcgg	ctaatatcca	120
ggaaactctc	aatcaagtca	ccgtcnatna	aacctgtggc	tggttctgtc	ttccgctcgg	180
tgtgaaagga	tctccagaag	gagtgtcga	tcttccccac	acttttgatg	actttattga	240
gtcgattctg	catgtccagc	aggaggttgt	accagctctc	tgacagttag	gtcaccagcc	300
ctatcatgcc	nttgaacgtg	ccgaagaaca	ccgagccttg	tgtggggggg	gnagtctcac	360
ccagattctg	cattaccaga	nagccgtggc	aaaaganatt	gacaactcgc	ccaggnggaa	420
aaagaacacc	tcctggaagt	gctngccgct	cctcgtccnt	tgggtggnng	gcntnccttt	480
t						481

&lt;210&gt; 86

&lt;211&gt; 472

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(472)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 86

aacatcttcc	tgtataatgc	tgtgtaatat	cgatccgatn	ttgtctgctg	agaattcatt	60
acttggaata	gcaacttnaa	gcctggacac	tggtattaaa	attcacaata	tgcaacactt	120
taaacagtgt	gtcaatctgc	tcccttactt	tgatcatcacc	agtctgggaa	taagggtatg	180
ccctattcac	acctgttaaa	agggcgctaa	gcatttttga	ttcaacatct	ttttttttga	240
cacaagtccg	aaaaaagcaa	aagtaaacag	ttnttaattt	gttagccaat	tcactttctt	300
catgggacag	agccatttga	tttaaaaagc	aaattgcata	atattgagct	ttgggagctg	360
atatntgagc	ggaagantag	cctttctact	tcaccagaca	caactccttt	catattggga	420
tgtttnacnaa	agttatgtct	cttacagatg	ggatgctttt	gtgggaattc	tg	472

&lt;210&gt; 87

&lt;211&gt; 413

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(413)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 87

agaaaccagt	atctctnaaa	acaacctctc	ataccttgtg	gacctaat	tgtgtgcgtg	60
tgtgtgtgcg	cgcataattat	atagacaggc	acatcttttt	tacttttgta	aaagcttatg	120
cctcttttgt	atctatatct	gtgaaagttt	taatgatctg	ccataatgtc	ttggggacct	180
ttgtcttctg	tgtaaatggg	actagagaaa	acacctatnt	tatgagtcaa	tctagttngt	240
tttattcgac	atgaaggaaa	tttccagatn	acaacactna	caaactctcc	cttgactagg	300
ggggacaaaag	aaaagcnaaa	ctgaacatna	gaaacaattn	cctggtgaga	aattncataa	360
acagaaattg	ggtngtatat	tgaaananng	catcattnaa	acgttttttt	ttt	413

&lt;210&gt; 88

&lt;211&gt; 448

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(448)

&lt;223&gt; n = A,T,C or G

<400> 88  
 cgcagcgggt cctctctatc tagctccagc ctctcgctg cccactccc cgcgccccgc 60  
 gtcctagccn accatggccg ggccccctgc cgccccctg ctctgtctgg ccctcctggc 120  
 cgtggccctg gccgtgagcc ccgcggcccg ctccagtcct ggcaagccgc cgcgccctgg 180  
 gggaggccca tggaccccg gcgtgaagaag aaggtgtgcg gcgtgcaact gactttgccc 240  
 tcggcnanta caacaaccc gcaacnactt ttaccnagcn cgcgctgcag gttgtgccgc 300  
 cccaancaaa ttgttactng gggtaantaa ttcttggaag ttgaacctgg gccaaacnng 360  
 tttaccagaa ccnagccaat tngaacaatt ncccctccat aacagcccct tttaaaaagg 420  
 gaancantcc tgntcttttc caaat ttt 448

<210> 89  
 <211> 463  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(463)  
 <223> n = A,T,C or G

<400> 89  
 gaattttgtg cactggccac tgtgatggaa ccattgggccc aggatgcttt gagtttatca 60  
 gtagtgattc tgccaaagt ggtgttgtaa catgagtatg taaaatgtca aaaaattagc 120  
 agaggtctag gtctgcatat cagcagacag ttgtccctg tattttgtag ccttgaagtt 180  
 ctcaagtaca agttnnttct gatgcgaagt tctnattcca gtgttttagt cctttgcatc 240  
 tttnatgttn agacttgccct ctntnaaatt gcttttgtnt tctgcaggta ctatctgtgg 300  
 ttttaacaaa tagaannact tctctgcttn gaanatttga atatcttaca tctnaaaatn 360  
 aattctctcc ccatannaaa acccangccc ttggganaat ttgaaaaang gntccttcnn 420  
 aattcnnana anttcagtn tcatacaaca naacngganc ccc 463

<210> 90  
 <211> 400  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(400)  
 <223> n = A,T,C or G

<400> 90  
 agggattgaa ggtctntnt actgtcggac tgttcancca ccaactctac aagttgctgt 60  
 cttccactca ctgtctgtaa gcntnttaac ccagactgta tcttcataaa tagaacaat 120  
 tcttcaccag tcacatcttc taggaccttt ttggattcag ttagtataag ctcttccact 180  
 tcctttgtta agacttcac tggtaaagtc ttaagttttg tagaaaggaa ttaattgtct 240  
 cgttctctaa caatgtcctc tccttgaagt atttggtga acaaccacc tnaagtcct 300  
 ttgtgcatcc attttaata tacttaatag ggcattggtn cactagggtta aattctgcaa 360  
 gagtcactctg tctgcaaaag ttgcgttagt atatctgcca 400

<210> 91  
 <211> 480  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(480)  
 <223> n = A,T,C or G

<400> 91  
 gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact 60

```

ggcttaccac  acatgggagc  agcatgccgt  agntatataa  ggtcattccc  tgagtccagc  120
atgcctcttt  gactaccgtg  tgccagtgtc  ggtgattctc  acacacctcc  nncgcctctt  180
tgtggaaaaa  ctggcacttg  nctggaacta  gcaagacatc  acttacaagt  tcacccacga  240
gacacttgaa  aggtgtaaca  aagcgactct  tgcattgctt  tttgtccctc  cggcaccagt  300
tgtcaatact  aaccgcgtgg  ttgacctcca  tcacatttgt  gatctgtagc  tctggataca  360
tctcctgaca  gtactgaaga  acttcttctt  ttgtttcaaa  agcaactctt  ggtgcctgtt  420
ngatcagggt  cccatttccc  agtccgaatg  ttcacatggc  atatnttact  tcccacaaaa  480

```

```

<210> 92
<211> 477
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(477)
<223> n = A,T,C or G

```

```

<400> 92
atacagccca  natcccacca  cgaagatgcg  cttgttgact  gagaacctga  tgcggtcact  60
ggtcccgtg  tagccccagc  gactctccac  ctgctggaag  cggttgatgc  tgcactcctt  120
cccacgcagg  cagcagcggg  gccgggtcaat  gaactccact  cgtggcttgg  ggttgacggt  180
taantgcagg  aagaggctga  ccacctcgcg  gtccaccagg  atgcccgact  gtgcgggacc  240
tgacagcгаа  ctctcgaatg  gtcatgagcg  ggaagcgaat  gangcccagg  gccttgccca  300
gaaccttccg  cctgttctct  ggcgtcacct  gcagctgctg  ccgctnacac  tcggcctcgg  360
accagcggac  aaacggcggt  gaacagccgc  acctcacgga  tgcccantgt  gtcgcgctcc  420
aggaacggcn  ccagcgtgtc  caggtcaatg  tcggtgaanc  ctccgcgggt  aatggcg  477

```

```

<210> 93
<211> 377
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(377)
<223> n = A,T,C or G

```

```

<400> 93
gaacggctgg  accttgctc  gcattgtgct  gctggcagga  ataccttggc  aagcagctcc  60
agtccgagca  gccccagacc  gctgccgccc  gaagctaagc  ctgcctctgg  ccttcccctc  120
cgctcaatg  cagaaccant  agtgggagca  ctgtgtttag  agttaagagt  gaacactgtn  180
tgattttact  tgggaatttc  ctctgttata  tagcttttcc  caatgctaag  ttccaaacaa  240
caacaacaaa  ataacatggt  tgccgtgtna  gttgtataaa  agtangtgat  tctgtatnta  300
aagaaaatat  tactgttaca  tatactgctt  gcaanttctg  tattttattg  tntctctggaa  360
ataaatatat  tattaata  377

```

```

<210> 94
<211> 495
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(495)
<223> n = A,T,C or G

```

```

<400> 94
ccctttgagg  ggtaggggtc  cagttcccag  tggaagaaac  aggccaggag  aantgcgtgc  60
cgagctgang  cagatttccc  acagtgaccc  cagagccctg  ggctatagtc  tctgaccctt  120
ccaaggaaa  accaccttct  ggggacatgg  gctggagggc  aggacctaga  ggcaccaagg  180
gaaggcccca  ttccggggct  gttccccgag  gaggaaggga  aggggctctg  tgtgcccccc  240

```

```

acgaggaana ggcctgant cctgggatca nacacccctt cacgtgtatc cccacacaaa 300
tgcaagctca ccaaggtccc ctctcagtc cttccctaca ccctgaacgg ncactggccc 360
acacccaccc agancancca cccgccatgg ggaatgtntc caaggaatcg cngggcaacg 420
tggaactctng tcccnaagg gggcagaatc tccaatagan gganngaacc cttgctnana 480
aaaaaaaaa aaaaaa 495

```

```

<210> 95
<211> 472
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(472)
<223> n = A,T,C or G

```

```

<400> 95
ggttacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc 60
cctctggaag ccttgccgag agcggacttt gtaattgttg gagaataact gctgaatttt 120
tagctgtttt gagttgattc gcaccactgc accacaactc aatatgaaaa ctatttnact 180
tatttattat cttgtgaaaa gtatacaatg aaaattttgt tcatactgta tttatcaagt 240
atgatgaaaa gcaatagata tatattcttt tattatgttn aattatgatt gccattatta 300
atcggcaaaa tgtggagtg atgttctttt cacagtaata tatgcctttt gtaacttcac 360
ttggttattt tattgtaaat gaattacaaa attcttaatt taagaaaatg gtangttata 420
tttanttcan taatttcttt ccttgtttac gttaattttg aaaagaatgc at 472

```

```

<210> 96
<211> 476
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(476)
<223> n = A,T,C or G

```

```

<400> 96
ctgaagcatt tcttcaaact tntctacttt tgtcattgat acctgtagta agttgacaat 60
gtggtgaaat ttcaaaatta tatgtaactt ctactagttt tactttctcc cccaagtctt 120
ttttaactca tgattttttac acacacaatc cagaacttat tatatagcct ctaagtcttt 180
attcttcaca gtagatgatg aaagagtcct ccagtgtctt gngcanaatg ttctagntat 240
agctggatac atacngtggg agttctataa actcatacct cagtgggact naaccaaatt 300
tgtgttagtc tcaattccta ccacactgag ggagcctccc aaatcactat attcttatct 360
gcaggtactc ctccagaaaa acngacaggg caggcttgca tgaaaaagtn acatctgcgt 420
tacaaagtct atcttctca nangtctgtt aaggaacaat ttaatcttct agcttt 476

```

```

<210> 97
<211> 479
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(479)
<223> n = A,T,C or G

```

```

<400> 97
actctttcta atgctgatat gatcttgagt ataagaatgc atatgtcact agaatggata 60
aaataatgct gcaaacttaa tgttcttatg caaatggaa cgctaataaa acacagctta 120
caatcgcaaa tcaaaactca caagtgtcga tctgttgtag atttagtgtg ataagactta 180
gattgtgctc cttcggatat gattgtttct canatcttgg gcaatnttcc ttagtcaaat 240
caggctacta gaattctgtt attggatatn tgagagcatg aaatttttaa naatacactt 300

```

<400>	98						
cttgt	cctccaacaa	aaccccttga	tcaagtttgt	ggcactgaca	atcagaccta		60
gttcc	tgtcatctat	tcgctactaa	atgcagactg	gagggggacca	aaaaggggca		120
ttcag	ctggattatt	ttggagcctg	caaatctatt	cctactttga	cggactttga		180
ttcag	tttcctctac	ggatgagaga	ctggctcaag	aatatcctca	tgcagcttta		240
ccact	ctgaacacgc	tggttatcta	gatgagaaca	gagaaataaa	gtcagaaaat		300
tggag	aaaagaggct	ttggctgggg	accatcccat	tgaaccttct	cttaaggact		360
aaaaa	ctaccacatg	ttgtgtatcc	tggtgcggcg	cgtttatgaa	ctgaccaccc		420
aataa	tcttgcagct	cctgaacctg	ctcctctgcg	a			461

<400> 99						
cgcg	gcaggtgttt	cctcgtaaccg	cagggccccc	tcccttcccc	aggcgtccct	60
cctct	gcgggcccca	ggaggagcgg	ctggcgggtg	gggggagtg	gaccaccct	120
agaaa	agccttctct	agcgatctga	gaggcgtgcc	ttgggggtac	c	171

<400> 100						
gcaag	tgcaactcca	gctggggccg	tgcggacgaa	gattctgcc	gcagttggtc	60
gcgac	gacggcgcg	gcgacagtcg	caggtgcagc	gcgggcgcct	ggggtcttgc	120
tgagc	tgacgccgca	gaggtcgtgt	cacgtccac	gaccttgacg	ccgtcgggga	180
ggaac	agagcccggt	gaagcgggag	gcctcgggga	gcccctcggg	aagggcggcc	240
gatac	gcaggtgcag	gtqgccgcc				269

<400>	101						
t	t	t	t	t	t	t	60
t	t	t	t	t	t	t	
t	t	t	t	t	t	t	120
t	t	t	t	t	t	t	180
t	t	t	t	t	t	t	240
t	t	t	t	t	t	t	300
t	t	t	t	t	t	t	360
t	t	t	t	t	t	t	405

```

<400> 102
+++++ 60

```

ggcacttaat	ccatttttat	ttcaaaatgt	ctacaaat	aatcccatta	tacgggtattt	120
tcaaaatcta	aattattcaa	attagccaaa	tccttaccaa	ataataccca	aaaatcaaaa	180
atatacttct	ttcagcaaac	ttgttacata	aattaaaaaa	atatatacgg	ctgggtgtttt	240
caaagtacaa	ttatcttaac	actgcaaac	ttttaaggaa	ctaaaaataa	aaaaaacact	300
ccgcaaaggt	taaagggaac	aacaaattct	tttacaacac	cattataaaa	atcatatctc	360
aaatcttagg	ggaatatata	cttcacacgg	gatcttaact	tttactcact	ttgtttattt	420
ttttaaacca	ttgtttgggc	ccaacacaat	ggaatcccc	ctggactagt		470

&lt;210&gt; 103

&lt;211&gt; 581

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 103

tttttttttt	ttttttttga	ccccctctt	ataaaaaaca	agttaccatt	ttattttact	60
tacacatatt	tattttataa	ttgggtattag	atattcaaaa	ggcagctttt	aaaatcaaac	120
taaatggaaa	ctgccttaga	tacataattc	ttaggaatta	gcttaaaatc	tgccataaagt	180
gaaaatcttc	tctagctctt	ttgactgtaa	atttttgact	cttgtaaaac	atccaaattc	240
atttttcttg	tctttaaaat	tatctaattc	ttccattttt	tccctattcc	aagtcaattt	300
gcttctctag	cctcatttcc	tagctcttat	ctactattag	taagtggctt	ttttcctaaa	360
agggaaaaca	ggaagagaaa	tggcacacaa	aacaaacatt	ttatattcat	atttctacct	420
acgttaataa	aatagcattt	tgtgaagcca	gctcaaaaga	aggcttagat	ccttttatgt	480
ccatttttagt	cactaaacga	tatcaaagtg	ccagaatgca	aaagggttgt	gaacatttat	540
tcaaaagcta	atataagata	tttcacatac	tcattctttct	g		581

&lt;210&gt; 104

&lt;211&gt; 578

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 104

tttttttttt	tttttttttt	tttttctctt	cttttttttt	gaaatgagga	tcgagttttt	60
cactctctag	atagggcatg	aagaaaactc	atctttccag	ctttaaaata	acaatcaaat	120
ctcttatgct	atatcatatt	ttaagttaaa	ctaataagtc	actggcttat	cttctcctga	180
aggaaatctg	ttcattcttc	tcattcatat	agttatatca	agtactacct	tgcatattga	240
gaggtttttt	ttctctattt	acacatatat	ttccatgtga	atttgtatca	aacctttatt	300
ttcatgcaaa	ctagaaaata	atgtttcttt	tgcataagag	aagagaacaa	tatagcatta	360
caaaaactgct	caaattgttt	gttaagttat	ccattataat	tagttggcag	gagctaatac	420
aaatcacatt	tacgacagca	ataataaaac	tgaagtacca	gttaaatatc	caaaaataatt	480
aaaggaacat	ttttagcctg	ggtataatta	gctaattcac	tttacaagca	tttattagaa	540
tgaattcaca	tggtattatt	cctagcccaa	cacaatgg			578

&lt;210&gt; 105

&lt;211&gt; 538

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 105

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gtcttgaaca	ccaatattaa	tttgaggaaa	atacaccaaa	atacattaag	taaatatttt	180
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agatatgttt	cctttgccaa	tattaaaaaa	ataataatgt	ttactactag	tgaaaccc	538

&lt;210&gt; 106

&lt;211&gt; 473

&lt;212&gt; DNA

&lt;213&gt; Homo sapien



## &lt;400&gt; 106

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## &lt;210&gt; 107

## &lt;211&gt; 1621

## &lt;212&gt; DNA

## &lt;213&gt; Homo sapien

## &lt;400&gt; 107

cgccatggca	ctgcagggca	tctcggtcat	ggagctgtcc	ggcctggccc	cgggcccgtt	60
ctgtgctatg	gtcctggctg	acttcggggc	gcgtgtggta	cgcgtggacc	ggcccggctc	120
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gttctacgag	ctgctgatca	aaggacttgg	actaaagtct	gatgaacttc	ccaatcagat	780
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agctagtctc	taacttccag	gcccacggct	caagtgaatt	tgaatactgc	atttacagtg	1200
tagagtaaca	cataacattg	tatgcatgga	aacatggagg	aacagtatta	cagtgtccta	1260
ccactctaata	caagaaaaga	attacagact	ctgattctac	agtgatgatt	gaattctaaa	1320
aatggttatc	attagggctt	ttgatttata	aaactttggg	tacttatact	aaattatggt	1380
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ttttgaatgg	gttctagtga	aaaaggaatg	atatattcct	gaagacatcg	atatacattt	1500
atttacactc	ttgattctac	aatgtagaaa	atgaggaaat	gccacaaatt	gtatggtgat	1560
aaaagtcacg	tgaacaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaa	1620
a						1621

## &lt;210&gt; 108

## &lt;211&gt; 382

## &lt;212&gt; PRT

## &lt;213&gt; Homo sapien

## &lt;400&gt; 108

Met	Ala	Leu	Gln	Gly	Ile	Ser	Val	Met	Glu	Leu	Ser	Gly	Leu	Ala	Pro
1				5					10					15	
Gly	Pro	Phe	Cys	Ala	Met	Val	Leu	Ala	Asp	Phe	Gly	Ala	Arg	Val	Val
			20					25					30		
Arg	Val	Asp	Arg	Pro	Gly	Ser	Arg	Tyr	Asp	Val	Ser	Arg	Leu	Gly	Arg
			35				40					45			
Gly	Lys	Arg	Ser	Leu	Val	Leu	Asp	Leu	Lys	Gln	Pro	Arg	Gly	Ala	Ala
	50					55				60					
Val	Leu	Arg	Arg	Leu	Cys	Lys	Arg	Ser	Asp	Val	Leu	Leu	Glu	Pro	Phe
65					70				75					80	

Arg Arg Gly Val Met Glu Lys Leu Gln Leu Gly Pro Glu Ile Leu Gln  
 85 90 95  
 Arg Glu Asn Pro Arg Leu Ile Tyr Ala Arg Leu Ser Gly Phe Gly Gln  
 100 105 110  
 Ser Gly Ser Phe Cys Arg Leu Ala Gly His Asp Ile Asn Tyr Leu Ala  
 115 120 125  
 Leu Ser Gly Val Leu Ser Lys Ile Gly Arg Ser Gly Glu Asn Pro Tyr  
 130 135 140  
 Ala Pro Leu Asn Leu Leu Ala Asp Phe Ala Gly Gly Gly Leu Met Cys  
 145 150 155 160  
 Ala Leu Gly Ile Ile Met Ala Leu Phe Asp Arg Thr Arg Thr Asp Lys  
 165 170 175  
 Gly Gln Val Ile Asp Ala Asn Met Val Glu Gly Thr Ala Tyr Leu Ser  
 180 185 190  
 Ser Phe Leu Trp Lys Thr Gln Lys Ser Ser Leu Trp Glu Ala Pro Arg  
 195 200 205  
 Gly Gln Asn Met Leu Asp Gly Gly Ala Pro Phe Tyr Thr Thr Tyr Arg  
 210 215 220  
 Thr Ala Asp Gly Glu Phe Met Ala Val Gly Ala Ile Glu Pro Gln Phe  
 225 230 235 240  
 Tyr Glu Leu Leu Ile Lys Gly Leu Gly Leu Lys Ser Asp Glu Leu Pro  
 245 250 255  
 Asn Gln Met Ser Met Asp Asp Trp Pro Glu Met Lys Lys Lys Phe Ala  
 260 265 270  
 Asp Val Phe Ala Lys Lys Thr Lys Ala Glu Trp Cys Gln Ile Phe Asp  
 275 280 285  
 Gly Thr Asp Ala Cys Val Thr Pro Val Leu Thr Phe Glu Glu Val Val  
 290 295 300  
 His His Asp His Asn Lys Glu Arg Gly Ser Phe Ile Thr Ser Glu Glu  
 305 310 315 320  
 Gln Asp Val Ser Pro Arg Pro Ala Pro Leu Leu Leu Asn Thr Pro Ala  
 325 330 335  
 Ile Pro Ser Phe Lys Arg Asp Pro Phe Ile Gly Glu His Thr Glu Glu  
 340 345 350  
 Ile Leu Glu Glu Phe Gly Phe Ser Arg Glu Glu Ile Tyr Gln Leu Asn  
 355 360 365  
 Ser Asp Lys Ile Ile Glu Ser Asn Lys Val Lys Ala Ser Leu  
 370 375 380

&lt;210&gt; 109

&lt;211&gt; 1524

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 109

ggcacgaggg tgcgccaggg cctgagcgga ggccgggggca gcctcgccag cggggggcccc 60  
 gggcctggcc atgcctcaact gagccagcgc ctgcgcctct acctcgccga cagctggaac 120  
 cagtgcgacc tagtggtctt cactgtcttc ctctggggcg tgggctgccg gctgaccccg 180  
 ggtttgtacc acctggggcg cactgtcttc tgcctcgact tcatggtttt cacggtgcgg 240  
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 gtggccacgg aggggctcct gagggcacgg gacagtgaact tcccaagtat cctgcgcgcg 420  
 gtcttctacc gtccttacct gcagatcttc gggcagattc cccaggagga catggacgtg 480  
 gccctcatgg agcacagcaa ctgctcgtcg gagcccggt tctgggcaca ccctcctggg 540  
 gccaggcggg gcacctgcgt ctccagtat gccaactggc tgggtgggtgct gctcctcgtc 600  
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 cgctcctctg tcaggcaatt gtgcaggcga ccccgaggcc cccagccgtc ctccccggcc 840  
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cgcgagtacg	aacagcgcct	gaaagtgcct	gagcgggagg	tccagcagtg	tagccgcgtc	1080
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cagaggaaaa	aaaaaaaaaa	aaaa				1524

<210> 110  
 <211> 3410  
 <212> DNA  
 <213> Homo sapien

<400> 110						
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aagctggacc	ggcaccaaa	ggctggcaga	aatgggcgcc	tggtgattc	ctaggcagtt	180
ggcggcagca	aggaggagag	gccgcagctt	ctggagcaga	gccgagacga	agcagttctg	240
gagtgcctga	acggccccct	gagccctacc	cgcctggccc	actatggtcc	agaggctgtg	300
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aaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaataa aaaaaaaaaa 3410

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<210> 111  
 <211> 1289  
 <212> DNA  
 <213> Homo sapien

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<400> 111
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ccatgcagtg cttcagcttc attaaagacca tgatgatcct cttcaatttg ctcatctttc 180
tgtgtggtgc agccctgttg gcagtgggca tctgggtgtc aatcgatggg gcatcctttc 240
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tcatcgcagc cggcgttgtg gtctttgtct ttggtttcct gggctgctat ggtgctaaga 360
ctgagagcaa gtgtgccctc gtgacgttct tcttcactct cctcctcatc ttcattgctg 420
aggttgcagc tgctgtggtc gccttggtgt acaccacaat ggctgagcac ttcctgacgt 480
tgctggtagt gcctgccatc aagaaagatt atggttccca ggaagacttc actcaagtgt 540
ggaacaccac catgaaaggg ctcaagtgtc gtggcttcac caactatacg gatthtgagg 600
actcacccta cttcaaagag aacagtgcct ttccccatt ctgttgcaat gacaacgtca 660
ccaacacagc caatgaaacc tgcaccaagc aaaaggctca cgaccaaaaa gtagagggtt 720
gcttcaatca gcttttgtat gacatccgaa ctaatgcagt caccgtgggt ggtgtggcag 780
ctggaattgg gggcctcgag ctggctgcca tgattgtgtc catgtatctg tactgcaatc 840
tacaataagt ccacttctgc ctctgccact actgctgcca catgggaact gtgaagaggc 900
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gaatggacct gccctttctg ctccagactt ggggctagat agggaccact ccttttagcg 1020
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gtagccagtt ctgttgccca ttccccagtt ctattaaacc cttgatatgc cccctaggcc 1140
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aagtgaatc agcagagcct ctgggtggat gtgtagaagg cacttcaaaa tgcataaacc 1260
tgttacaatg ttaaaaaaaa aaaaaaaaaa 1289

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<210> 112  
 <211> 315  
 <212> PRT  
 <213> Homo sapien

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<400> 112
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Leu Gly Pro Lys Ile Val Ile Val Ser Lys Met Met Lys Asp Val Phe
20 25 30
Phe Phe Leu Phe Phe Leu Gly Val Trp Leu Val Ala Tyr Gly Val Ala
35 40 45
Thr Glu Gly Leu Leu Arg Pro Arg Asp Ser Asp Phe Pro Ser Ile Leu
50 55 60
Arg Arg Val Phe Tyr Arg Pro Tyr Leu Gln Ile Phe Gly Gln Ile Pro
65 70 75 80
Gln Glu Asp Met Asp Val Ala Leu Met Glu His Ser Asn Cys Ser Ser
85 90 95
Glu Pro Gly Phe Trp Ala His Pro Pro Gly Ala Gln Ala Gly Thr Cys
100 105 110
Val Ser Gln Tyr Ala Asn Trp Leu Val Val Leu Leu Val Ile Phe

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115	120	125
Leu Leu Val Ala Asn Ile	Leu Leu Val Asn Leu	Leu Ile Ala Met Phe
130	135	140
Ser Tyr Thr Phe Gly Lys Val	Gln Gly Asn Ser Asp	Leu Tyr Trp Lys
145	150	155
Ala Gln Arg Tyr Arg Leu Ile	Arg Glu Phe His Ser	Arg Pro Ala Leu
165	170	175
Ala Pro Pro Phe Ile Val Ile	Ser His Leu Arg Leu Leu	Leu Arg Gln
180	185	190
Leu Cys Arg Arg Pro Arg Ser	Pro Gln Pro Ser Ser	Pro Ala Leu Glu
195	200	205
His Phe Arg Val Tyr Leu Ser	Lys Glu Ala Glu Arg	Lys Leu Leu Thr
210	215	220
Trp Glu Ser Val His Lys Glu	Asn Phe Leu Leu Ala	Arg Ala Arg Asp
225	230	235
Lys Arg Glu Ser Asp Ser Glu	Arg Leu Lys Arg Thr Ser	Gln Lys Val
245	250	255
Asp Leu Ala Leu Lys Gln Leu	Gly His Ile Arg Glu Tyr	Glu Gln Arg
260	265	270
Leu Lys Val Leu Glu Arg Glu	Val Gln Gln Cys Ser Arg	Val Leu Gly
275	280	285
Trp Val Ala Glu Ala Leu Ser	Arg Ser Ala Leu Leu	Pro Pro Gly Gly
290	295	300
Pro Pro Pro Pro Asp Leu	Pro Gly Ser Lys Asp	
305	310	315

<210> 113  
 <211> 553  
 <212> PRT  
 <213> Homo sapien

<400> 113
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20 25 30
Ala Ala Gly Ile Thr Tyr Val Pro Leu Leu Leu Glu Val Gly Val
35 40 45
Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly
50 55 60
Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly
65 70 75 80
Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile
85 90 95
Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu
100 105 110
Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly
115 120 125
Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu
130 135 140
Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala
145 150 155 160
Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr
165 170 175
Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu
180 185 190
Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu
195 200 205
Thr Cys Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly
210 215 220
Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His
225 230 235 240

Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu  
 245 250 255  
 Leu Pro Arg Leu His Gln Leu Cys Cys Arg Met Pro Arg Thr Leu Arg  
 260 265 270  
 Arg Leu Phe Val Ala Glu Leu Cys Ser Trp Met Ala Leu Met Thr Phe  
 275 280 285  
 Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu Gly Leu Tyr Gln Gly Val  
 290 295 300  
 Pro Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly  
 305 310 315 320  
 Val Arg Met Gly Ser Leu Gly Leu Phe Leu Gln Cys Ala Ile Ser Leu  
 325 330 335  
 Val Phe Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg  
 340 345 350  
 Ala Val Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala  
 355 360 365  
 Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu  
 370 375 380  
 Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala  
 385 390 395 400  
 Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly  
 405 410 415  
 Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu  
 420 425 430  
 Pro Gly Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala  
 435 440 445  
 Gly Gly Ser Gly Leu Leu Pro Pro Pro Ala Leu Cys Gly Ala Ser  
 450 455 460  
 Ala Cys Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala  
 465 470 475 480  
 Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp  
 485 490 495  
 Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser  
 500 505 510  
 Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala  
 515 520 525  
 Gly Leu Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp  
 530 535 540  
 Lys Ser Asp Leu Ala Lys Tyr Ser Ala  
 545 550

<210> 114  
 <211> 241  
 <212> PRT  
 <213> Homo sapien

<400> 114  
 Met Gln Cys Phe Ser Phe Ile Lys Thr Met Met Ile Leu Phe Asn Leu  
 1 5 10 15  
 Leu Ile Phe Leu Cys Gly Ala Ala Leu Leu Ala Val Gly Ile Trp Val  
 20 25 30  
 Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser  
 35 40 45  
 Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly  
 50 55 60  
 Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr  
 65 70 75 80  
 Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Phe Ile Leu Leu Leu Ile  
 85 90 95  
 Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr  
 100 105 110  
 Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys

115	120	125
Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met		
130	135	140
Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp		
145	150	155
Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn		
165	170	175
Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala		
180	185	190
His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile		
195	200	205
Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly		
210	215	220
Leu Glu Leu Ala Ala Met Ile Val Ser Met Tyr Leu Tyr Cys Asn Leu		
225	230	235
Gln		240

<210> 115  
 <211> 366  
 <212> DNA  
 <213> Homo sapien

<400> 115  
 gctctttctc tcccctctc tgaatttaac tctttcaact tgcaatttgc aaggattaca 60  
 catttcactg tgatgtatat tgtgttgcaa aaaaaaaaaa gtgtctttgt ttaaaattac 120  
 ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga 180  
 actggtagaa aaacatctga agagctagtc tatcagcatc tgacagggtga attggatggg 240  
 tctcagaacc atttcaccca gacagcctgt ttctatcctg ttttaataaat tagtttgggt 300  
 tctctacatg cataacaaac cctgctccaa tctgtcacat aaaagtctgt gacttgaagt 360  
 ttagtc 366

<210> 116  
 <211> 282  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(282)  
 <223> n = A,T,C or G

<400> 116  
 acaaagatga accatttcct atattatagc aaaattaaaa tctacccgta ttctaattatt 60  
 gagaaatgag atnaaacaca atnttataaa gtctacttag agaagatcaa gtgacctcaa 120  
 agactttact attttcatat ttaagacac atgattttatc ctatttttagt aacctgggtc 180  
 atacgttaaa caaaggataa tgtgaacagc agagaggatt tgttggcaga aaatctatgt 240  
 tcaatctnga actatctana tcacagacat ttctatttcct tt 282

<210> 117  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(305)  
 <223> n = A,T,C or G

<400> 117  
 acacatgtcg cttcactgcc ttcttagatg cttctgggtca acatanagga acagggacca 60  
 tattttatcct ccctcctgaa acaattgcaa aataanacaa aatatatgaa acaattgcaa 120

aataaggcaa aatatatgaa acaacagggtc tcgagatatt ggaaatcagt caatgaagga	180
tactgatccc tgatcactgt cctaattgcag gatgtgggaa acagatgagg tcacctctgt	240
gactgcccc gcttactgcc tgtagagagt ttctangctg cagttcagac agggagaaat	300
tggt	305

<210> 118  
 <211> 71  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(71)  
 <223> n = A,T,C or G

<400> 118	
accaaggtgt ntgaatctct gacgtgggga tctctgattc ccgcacaatc tgagtggaaa	60
aantcctggg t	71

<210> 119  
 <211> 212  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(212)  
 <223> n = A,T,C or G

<400> 119	
actccggttg gtgtcagcag cacgtggcat tgaacatngc aatgtggagc ccaaaccaca	60
gaaaatgggg tgaaattggc caactttcta tnaacttatg ttggcaantt tgccaccaac	120
agtaagctgg cccttctaataaaaagaaaat tgaaagggtt ctcactaanc ggaattaant	180
aatggantca aganactccc aggcctcagc gt	212

<210> 120  
 <211> 90  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(90)  
 <223> n = A,T,C or G

<400> 120	
actcgttgca natcaggggc cccccagagt caccgttgca ggagtccttc tggctcttgcc	60
ctccgccggc gcagaacatg ctgggggtgt	90

<210> 121  
 <211> 218  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(218)  
 <223> n = A,T,C or G

<400> 121	
tgtancgtga anaccacaga nagggttgct aaaaatggag aanccttgaa gtcattttga	60
gaataagatt tgctaaaaga tttggggcta aaacatgggt attgggagac atttctgaag	120



atatncangt aaattangga atgaattcat ggttcttttg ggaattcctt tacgatngcc 180  
agcatanact tcatgtgggg atancagcta cccttgta 218

<210> 122  
<211> 171  
<212> DNA  
<213> Homo sapien

<400> 122  
taggggtgta tgcaactgta aggacaaaaa ttgagactca actggcttaa ccaataaagg 60  
catttgtag ctcatggaac aggaagtcgg atggtggggc atcttcagt ctgcatgagt 120  
caccaccccg gcgggggtcat ctgtgccaca ggtccctgtt gacagtgcgg t 171

<210> 123  
<211> 76  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(76)  
<223> n = A,T,C or G

<400> 123  
tgtagcgtga agacnacaga atggtgtgtg ctgtgctatc caggaacaca tttattatca 60  
ttatcaanta ttgtgt 76

<210> 124  
<211> 131  
<212> DNA  
<213> Homo sapien

<400> 124  
acctttcccc aaggccaatg tcctgtgtgc taaactggccg gctgcaggac agctgcaatt 60  
caatgtgctg ggtcatatgg aggggaggag actctaaaat agccaatttt attctcttgg 120  
ttaagatttg t 131

<210> 125  
<211> 432  
<212> DNA  
<213> Homo sapien

<400> 125  
actttatcta ctggctatga aatagatggg ggaaaattgc gttaccaact ataccactgg 60  
cttgaaaaag aggtgatagc tcttcagagg acttgtgact ttggtcaga tgctgaagaa 120  
ctacagtctg catttggcag aaatgaagat gaatttggat taaatgagga tgctgaagat 180  
ttgcctcacc aaacaaaagt gaaacaactg agagaaaatt ttcaggaaaa aagacagtgg 240  
ctcttgaagt atcagtcact tttgagaatg tttcttagtt actgcatact tcatggatcc 300  
catggtgggg gtcttgcatc tgtaagaatg gaattgattt tgcttttgca agaattctag 360  
caggaaacat cagaaccact attttctagc cctctgtcag agcaaaccctc agtgcctctc 420  
ctctttgctt gt 432

<210> 126  
<211> 112  
<212> DNA  
<213> Homo sapien

<400> 126  
acacaacttg aatagtaaaa tagaaactga gctgaaattt ctaattcact ttctaaccat 60  
agtaagaatg atatttcccc ccagggatca ccaaatattt ataaaaattt gt 112

<210> 127

<211> 54  
 <212> DNA  
 <213> Homo sapien

<400> 127  
 accacgaaac cacaacaag atggaagcat caatccactt gccaaagcaca gcag 54

<210> 128  
 <211> 323  
 <212> DNA  
 <213> Homo sapien

<400> 128  
 acctcattag taattgtttt gttgtttcat ttttttctaa tgtctcccct ctaccagctc 60  
 acctgagata acagaatgaa aatggaagga cagccagatt tctcctttgc tctctgctca 120  
 ttctctctga agtctagggt acccattttg gggacccatt ataggcaata aacacagttc 180  
 ccaaagcatt tggacagttt cttgttgtgt tttagaatgg ttttcctttt tcttagcctt 240  
 ttctgcaaa aggtcactc agtcccttgc ttgtcagtg gactgggctc cccagggcct 300  
 aggtgcctt cttttccatg tcc 323

<210> 129  
 <211> 192  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(192)  
 <223> n = A,T,C or G

<400> 129  
 acatacatgt gtgtatatatt ttaaataatca cttttgtatc actctgactt tttagcatac 60  
 tgaaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcatc 120  
 tagcacattc atctgtgata naaagatagg tgagtttcat ttccttcacg ttggccaatg 180  
 gataaacaat gt 192

<210> 130  
 <211> 362  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(362)  
 <223> n = A,T,C or G

<400> 130  
 ccctttttta tggaaatgagt agactgtatg tttgaanatt tanccacaac ctctttgaca 60  
 tataatgacg caacaaaaag gtgctgttta gtcctatggg tcagtttatg cccctgacaa 120  
 gtttccattg tgttttgccc atcttctggc taatcgtggg atcctccatg ttattagtaa 180  
 ttctgtattc cattttggtt acgcctggta gatgtaacct gctangaggc taactttata 240  
 cttatttaaa agctcttatt ttgtgggtcat taaaatggca atttatgtgc agcactttat 300  
 tgacgcagga agcacgtgtg ggttggttgg aaagctctt gctaattcta aaaagtaatg 360  
 gg 362

<210> 131  
 <211> 332  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature

&lt;222&gt; (1)...(332)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 131

ctttttgaaa gatcgtgtcc actcctgtgg acatcttggt ttaatggagt ttcccatgca	60
gtangactgg tatgggttgca gctgtccaga taaaaacatt tgaagagctc caaaatgaga	120
gttctcccag gttcgccctg ctgctccaag tctcagcagc agcctctttt aggaggcatc	180
ttctgaacta gattaaggca gcttgtaaat ctgatgtgat ttgggtttatt atccaactaa	240
cttccatctg ttatcactgg agaaagccca gactcccan gacnggtacg gattgtgggc	300
atanaaggat tgggtgaagc tggcgttggt gt	332

&lt;210&gt; 132

&lt;211&gt; 322

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(322)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 132

acttttgcca ttttgtatat ataaacaatc ttgggacatt ctctgaaaa ctaggtgtcc	60
agtggctaag agaactcgat ttcaagcaat tctgaaagga aaaccagcat gacacagaat	120
ctcaaatcc caaacagggg ctctgtggga aaaatgaggg aggaccttg tatctcgggt	180
tttagcaagt taaaatgaan atgacaggaa aggcttattt atcaacaaag agaagagttg	240
ggatgcttct aaaaaaaact ttggtagaga aaataggaat gctnaatcct agggaagcct	300
gtaacaatct acaattgggtc ca	322

&lt;210&gt; 133

&lt;211&gt; 278

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(278)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 133

acaagccttc acaagtttaa ctaaattggg attaatcttt ctgtanttat ctgcataatt	60
cttgtttttc tttccatctg gctcctgggt tgacaatttg tggaaacaac tctattgcta	120
ctatttataa aaaatcacaa atctttccct ttaagctatg ttnaattcaa actattcctg	180
ctattcctgt tttgtcaaag aaattatatt tttcaaaata tgtntatttg tttgatgggt	240
cccacgaaac actaataaaa accacagaga ccagcctg	278

&lt;210&gt; 134

&lt;211&gt; 121

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(121)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 134

gtttanaaaa cttgtttagc tccatagagg aaagaatgtt aaactttgta ttttaaaaca	60
tgattctctg aggttaaaact tggttttcaa atgttatttt tacttgtatt ttgcttttgg	120
t	121

&lt;210&gt; 135

<211> 350  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(350)  
 <223> n = A,T,C or G

<400> 135  
 acttanaaacc atgcctagca catcagaatc cctcaaagaa catcagtata atcctataacc 60  
 atancaagtg gtgactggtt aagcgtgcga caaaggtcag ctggcacatt acttggtgac 120  
 aaacttgata cttttgttct aagtaggaac tagtatacag tncctaggan tggtagtcca 180  
 ggggtgcccc caactcctgc agcgcctcct ctgtgccagn ccctgnaagg aactttcgct 240  
 ccacctcaat caagccctgg gccatgctac ctgcaattgg ctgaacaaac gtttgctgag 300  
 ttccaagga tgcaaagcct ggtgctcaac tcctggggcg tcaactcagt 350

<210> 136  
 <211> 399  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(399)  
 <223> n = A,T,C or G

<400> 136  
 tgtaccgtga agacgacaga agttgcatgg cagggacagg gcagggccga ggccagggtt 60  
 gctgtgattg tatccgaata ntccctcgtga gaaaagataa tgagatgacg tgagcagcct 120  
 gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgcc ttggctctga 180  
 cctggcggcc agccagccag ccacaggtgg gcttcttcct tttgtggtga caacnccaag 240  
 aaaactgcag aggccagggt tcaggtgtna gtgggtangt gaccataaaa caccaggtgc 300  
 tcccaggaac ccgggcaaag gccatcccca cctacagcca gcatgccac tggcgtgatg 360  
 ggtgcagang gatgaagcag ccagntgttc tgctgtggt 399

<210> 137  
 <211> 165  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(165)  
 <223> n = A,T,C or G

<400> 137  
 actgggtgtgg tngggggtga tgctggtggt anaagttgan gtgacttcan gatggtgtgt 60  
 ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga 120  
 ttggctggtc ccactggtgg tcaactgtcat tgggtggggt cctgt 165

<210> 138  
 <211> 338  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(338)  
 <223> n = A,T,C or G

<400> 138

actcactgga	atgccacatt	cacaacagaa	tcagaggtct	gtgaaaacat	taatggctcc	60
ttaactttct	cagtaagaat	cagggacttg	aaatggaaac	gttaacagcc	acatgcccac	120
tgctgggcag	tctcccatgc	cttccacagt	gaaagggctt	gagaaaaatc	acatccaatg	180
tcatgtgttt	ccagccacac	caaaaggtgc	ttgggggtgga	gggctggggg	catananggt	240
cangcctcag	gaagcctcaa	gttccattca	gctttgccac	tgtacattcc	ccatntttaa	300
aaaaactgat	gccttttttt	tttttttttg	taaaattc			338

<210> 139  
 <211> 382  
 <212> DNA  
 <213> Homo sapien

<400> 139						
gggaatcttg	gtttttggca	tctggtttgc	ctatagccga	ggccactttg	acagaacaaa	60
gaaagggact	tcgagtaaga	aggtgattta	cagccagcct	agtgcccgaa	gtgaaggaga	120
attcaaacag	acctcgatcat	tcctgggtgtg	agcctggctg	gctcaccgcc	tatcatctgc	180
atttgccctta	ctcaggtgct	accggactct	ggcccctgat	gtctgtagtt	tcacaggatg	240
ccttatttgt	cttctacacc	ccacagggcc	ccctacttct	tcggatgtgt	ttttaataat	300
gtcagctatg	tgccccatcc	tccttcatgc	cctccctccc	tttctacca	ctgctgagtg	360
gcctggaact	tgtttaaagt	gt				382

<210> 140  
 <211> 200  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(200)  
 <223> n = A,T,C or G

<400> 140						
accaaaactt	ctttctgttg	tgttngattt	tactataggg	gtttngcttn	ttctaaanat	60
acttttcatt	taacancctt	tgtaagtgt	caggctgcac	tttgctccat	anaattattg	120
ttttcacatt	tcaacttgta	tggtttgtc	tcttanagca	ttggtgaaat	cacatatttt	180
atattcagca	taaaggagaa					200

<210> 141  
 <211> 335  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(335)  
 <223> n = A,T,C or G

<400> 141						
actttatttt	caaaacactc	atatgttgca	aaaaacacat	agaaaaataa	agtttggtgg	60
gggtgctgac	taaacttcaa	gtcacagact	tttatgtgac	agattggagc	agggtttggt	120
atgcatgtag	agaacccaaa	ctaattttatt	aaacaggata	gaaacaggct	gtctgggtga	180
aatgggttctg	agaaccatcc	aattcacctg	tcagatgctg	atanactagc	tcttcagatg	240
tttttctacc	agttcagaga	tnggttaatg	actantttcca	atggggaaaa	agcaagatgg	300
attcacaac	caagtaattt	taaacaaaga	cactt			335

<210> 142  
 <211> 459  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature

&lt;222&gt; (1)...(459)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 142

accagggttaa	tattgccaca	tatatccttt	ccaattgcgg	gctaaacaga	cgtgtattta	60
gggttggtta	aagacaacc	agcttaatat	caagagaaat	tgtgaccttt	catggagtat	120
ctgatggaga	aaacactgag	ttttgacaaa	tcttatttta	ttcagatagc	agtctgatca	180
cacatgggtcc	aacaacactc	aaataataaa	tcaaataatna	tcagatgtta	aagattggtc	240
ttcaaacatc	atagccaatg	atgccccgct	tgccctataat	ctctccgaca	taaaaccaca	300
tcaacacctc	agtggccacc	aaaccattca	gcacagcttc	cttaactgtg	agctgtttga	360
agctaccagt	ctgagcacta	ttgactatnt	ttttcangct	ctgaatagct	ctagggatct	420
cagcanggggt	gggaggaacc	agctcaacct	tggcgtant			459

&lt;210&gt; 143

&lt;211&gt; 140

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 143

acatttcctt	ccaccaagtc	aggactcctg	gcttctgtgg	gagttcttat	cacctgaggg	60
aaatccaaac	agtctctcct	agaaaggaat	agtgtcacca	acccaccca	tctccctgag	120
accatccgac	ttccctgtgt					140

&lt;210&gt; 144

&lt;211&gt; 164

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(164)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 144

acttcagtaa	caacatacaa	taacaacatt	aagtgtatat	tgccatcttt	gtcattttct	60
atctatacca	ctctcccttc	tgaaaacaan	aatcactanc	caatcactta	tacaaatttg	120
aggcaattaa	tccatatattg	ttttcaataa	ggaaaaaaag	atgt		164

&lt;210&gt; 145

&lt;211&gt; 303

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(303)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 145

acgtagacca	tccaactttg	tatttgtaat	ggcaaacatc	cagnagcaat	tcctaaacaa	60
actggagggt	atttataccc	aattatccca	ttcattaaca	tgccctcctc	ctcaggctat	120
gcaggacagc	tatcataagt	cggcccaggc	atccagatac	taccatttgt	ataaacttca	180
gtaggggagt	ccatccaagt	gacaggtcta	atcaaaggag	gaaatggaac	ataagcccag	240
tagtaaaatn	ttgcttagct	gaaacagcca	caaaagactt	accgccgtgg	tgattaccat	300
caa						303

&lt;210&gt; 146

&lt;211&gt; 327

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

<221> misc\_feature  
 <222> (1)...(327)  
 <223> n = A,T,C or G

<400> 146  
 actgcagctc aattagaagt ggtctctgac tttcatcanc ttctccctgg gctccatgac 60  
 actggcctgg agtgactcat tgctctggtt ggttgagaga gctcctttgc caacaggcct 120  
 ccaagtcagg gctgggattt gtttcctttc cacattctag caacaatatg ctggccactt 180  
 cctgaacagg gaggggtggga ggagccagca tggaacaagc tgccactttc taaagtagcc 240  
 agacttgccc ctgggcctgt cacacctact gatgaccttc tgtgcctgca ggatggaatg 300  
 taggggtgag ctgtgtgact ctatggt 327

<210> 147  
 <211> 173  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(173)  
 <223> n = A,T,C or G

<400> 147  
 acattgtttt tttgagataa agcattgana gagctctcct taacgtgaca caatggaagg 60  
 actggaacac ataccacat cttgttctg agggataatt ttctgataaa gtcttgctgt 120  
 atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gtt 173

<210> 148  
 <211> 477  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(477)  
 <223> n = A,T,C or G

<400> 148  
 acaaccactt tatctcatcg aatttttaac ccaaactcac tcaactgtgcc tttctatcct 60  
 atgggatata ttatttgatg ctccatttca tcacacatat atgaataata cactcatact 120  
 gccctactac ctgctgcaat aatcacattc ccttcctgtc ctgaccctga agccattggg 180  
 gtggtcctag tgccatcag tccangcctg caccttgagc ccttgagctc cattgctcac 240  
 nccanccac ctacccgacc ccatcctctt acacagctac ctccctgctc tctaacccca 300  
 tagattatnt ccaaattcag tcaattaagt tactattaac actctaccgg acatgtccag 360  
 caccactggg aagccttctc cagccaacac acacacacac acacncacac acacacatat 420  
 ccaggcacag gctacctcat cttcacaatc acccctttaa ttaccatgct atggtgg 477

<210> 149  
 <211> 207  
 <212> DNA  
 <213> Homo sapien

<400> 149  
 acagttgtat tataatatca agaaataaac ttgcaatgag agcatttaag agggaagaac 60  
 taacgtatatt tagagagcca aggaagggtt ctgtggggag tgggatgtaa ggtggggcct 120  
 gatgataaat aagagtcagc caggtaagtg ggtggtgtgg tatgggcaca gtgaagaaca 180  
 tttcaggcag agggaacagc agtgaaa 207

<210> 150  
 <211> 111  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(111)  
 <223> n = A,T,C or G

<400> 150  
 accttgattt cattgctgct ctgatggaaa cccaactatc taatttagct aaaacatggg 60  
 cacttaaagt tggtcagtgt ttggacttgt taactantgg catctttggg t 111

<210> 151  
 <211> 196  
 <212> DNA  
 <213> Homo sapien

<400> 151  
 agcgcggcag gtcattattga acattccaga tacctatcat tactcgatgc tgttgataac 60  
 agcaagatgg ctttgaactc agggtcacca ccagctattg gaccttacta tgaaaaccat 120  
 ggataccaac cggaataccc ctatcccgca cagccactg tggccccac tgtctacgag 180  
 gtgcatccgg ctcaagt 196

<210> 152  
 <211> 132  
 <212> DNA  
 <213> Homo sapien

<400> 152  
 acagcacttt cacatgtaag aaggagaaaa ttctaaatg taggagaaag ataacagaac 60  
 cttccctttt tcatctagt gtggaaacct gatgctttat gttgacagga atagaaccag 120  
 gagggagttt gt 132

<210> 153  
 <211> 285  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(285)  
 <223> n = A,T,C or G

<400> 153  
 acaanaccca nganaggcca ctggccgtgg tgtcatggcc tccaaacatg aaagtgtcag 60  
 cttctgctct tatgtctca tctgacaact ctttaccatt tttatcctcg ctcagcagga 120  
 gcacatcaat aaagtccaaa gtcttgact tggccttggc ttggaggag tcatcaacac 180  
 cctggctagt gaggggtgagg cgccgtcctt ggatgacggc atctgtgaag tcgtgcacca 240  
 gtctgcaggc cctgtggaag cgccgtccac acggagtnag gaatt 285

<210> 154  
 <211> 333  
 <212> DNA  
 <213> Homo sapien

<400> 154  
 accacagtcc tgttgggcca gggttctatg accctttctg tgaaaagcca tattatcacc 60  
 accccaaatt ttctcttaaa tatctttaac tgaaggggtc agcctcttga ctgcaaagac 120  
 cctaagccgg ttacacagct aactccact ggccctgatt tgtgaaattg ctgctgcctg 180  
 attggcacag gagtcgaagg tgttcagctc cctcctccg tggaaacgaga ctctgatttg 240  
 agtttcacaa attctcgggc cactcgtca ttgctcctct gaaataaaat ccggagaatg 300  
 gtcaggcctg tctcatccat atggatcttc cgg 333

<210> 155



<211> 308  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(308)  
 <223> n = A,T,C or G

<400> 155  
 actggaaata ataaaaccca catcacagtg ttgtgtcaaa gatcatcagg gcatggatgg 60  
 gaaagtgcct tgggaactgt aaagtgccta acacatgac gatgattttt gttataatat 120  
 ttgaatcacg gtgcatacaa actctcctgc ctgctcctcc tgggccccag cccagcccc 180  
 atcacagctc actgctctgt tcatccaggc ccagcatgta gtggctgatt cttcttggt 240  
 gcttttagcc tccanaagtt tctctgaagc caaccaaacc tctangtgta aggcattgctg 300  
 gccctggt 308

<210> 156  
 <211> 295  
 <212> DNA  
 <213> Homo sapien

<400> 156  
 accttgctcg gtgcttgga catattagga actcaaaata tgagatgata acagtgccta 60  
 ttattgatta ctgagagaac tgtagacat ttagttgaag attttctaca caggaactga 120  
 gaataggaga ttatgtttgg cctcatatt ctctcctatc ctcttgccct cattctatgt 180  
 ctaatatatt ctcaatcaaa taaggttagc ataatcagga aatcgaccaa ataccaatat 240  
 aaaaccagat gtctatcctt aagattttca aatagaaaac aaattaacag actat 295

<210> 157  
 <211> 126  
 <212> DNA  
 <213> Homo sapien

<400> 157  
 acaagtttaa atagtgtctg cactgtgcat gtgctgaaat gtgaaatcca ccacatttct 60  
 gaagagcaaa acaaattctg tcatgtaatc tctatcttgg gtctgtggga tatctgtccc 120  
 cttagt 126

<210> 158  
 <211> 442  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(442)  
 <223> n = A,T,C or G

<400> 158  
 acccactggt cttggaaaca cccatcctta atacgatgat ttttctgtcg tgtgaaaatg 60  
 aanccagcag gctgcccta gtcagtcctt ccttcagag aaaaagagat ttgagaaaagt 120  
 gctgtggtaa ttcaccatta atttcctccc ccaaactctc tgagtcttcc cttaatattt 180  
 ctggtggttc tgaccaaagc aggtcatggt ttgttgagca tttgggatcc cagtgaagta 240  
 natgtttgta gccttgcata cttagccctt cccacgcaca aacggagtgg cagagtgggtg 300  
 ccaaccctgt tttcccagtc cacgtagaca gattcacagt gcggaattct ggaagctgga 360  
 nacagacggg ctctttgcag agccgggaact ctgagangga catgagggcc tctgcctctg 420  
 tgttcattct ctgatgtcct gt 442

<210> 159  
 <211> 498  
 <212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(498)

<223> n = A,T,C or G

<400> 159

acttccaggt	aacgttggtg	tttccgttga	gcctgaactg	atgggtgacg	ttgtagggtc	60
tccaacaaga	actgaggttg	cagagcgggt	agggagaggt	gctgttccag	ttgcacctgg	120
gctgctgtgg	actgttggtg	attcctcact	acggcccaag	gttgtggaac	tggcanaaag	180
gtgtgtgtgt	gganttgagc	tcgggcggct	gtggtagggt	gtgggtctct	caacaggggc	240
tgtgtgtgtg	ccgggaggtg	aangtgttgt	gtcacttgag	cttggccagc	tctggaaagt	300
antanattct	tcctgaaggc	cagcgttgtg	ggagctggca	ngggtcantg	ttgtgtgtaa	360
cgaaccagtg	ctgctgtggg	tgggtgtana	tcctccacaa	agcctgaagt	tatggtgtcn	420
tcaggtaana	atgtgttttc	agtgtccctg	ggcngctgtg	gaaggttgta	nattgtcacc	480
aagggaataa	gctgtggt					498

<210> 160

<211> 380

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(380)

<223> n = A,T,C or G

<400> 160

acctgcatcc	agcttccctg	ccaaactcac	aaggagacat	caacctctag	acagggaaac	60
agcttcagga	tacttccagg	agacagagcc	accagcagca	aaacaaatat	tcccatgcct	120
ggagcatggc	atagaggaag	ctganaaatg	tggggtctga	ggaagccatt	tgagtctggc	180
cactagacat	ctcatcagcc	acttgtgtga	agagatgccc	catgacccca	gatgcctctc	240
ccacccttac	ctccatctca	cacacttgag	ctttccactc	tgtataattc	taacatcctg	300
gagaaaaatg	gcagtttgac	cgaacctgtt	cacaacggta	gaggctgatt	tctaacgaaa	360
cttgtagaat	gaagcctgga					380

<210> 161

<211> 114

<212> DNA

<213> Homo sapien

<400> 161

actccacatc	ccctctgagc	aggcgggtgt	cgttcaaggt	gtatttggcc	ttgcctgtca	60
cactgtccac	tggcccttta	tccacttggt	gcttaatccc	tcgaaagagc	atgt	114

<210> 162

<211> 177

<212> DNA

<213> Homo sapien

<400> 162

actttctgaa	tcgaatcaaa	tgatacttag	tgtagtttta	atatacctcat	atatatcaaa	60
gttttactac	tctgataatt	ttgtaaacca	ggtaaccaga	acatccagtc	atacagcttt	120
tggtgatata	taacttggca	ataaccaggt	ctggtgatata	ataaaactac	tcactgt	177

<210> 163

<211> 137

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature  
 <222> (1)...(137)  
 <223> n = A,T,C or G

<400> 163

catttataca	gacaggcgtg	aagacattca	cgacaaaaac	gcgaaattct	atcccgtagc	60
canagaaggc	agctacggct	actcctacat	cctggcgtgg	gtggccttcg	cctgcacctt	120
catcagcggc	atgatgt					137

<210> 164  
 <211> 469  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(469)  
 <223> n = A,T,C or G

<400> 164

cttatcacaa	tgaatgttct	cctgggcagc	gttgtgatct	ttgccacctt	cgtgacttta	60
tgcaatgcat	catgctattt	cataccta	gagggagttc	caggagattc	aaccaggaaa	120
tgcatggatc	tcaaaggaaa	caaacaccca	ataaactcgg	agtggcagac	tgacaactgt	180
gagacatgca	cttgctacga	aacagaaatt	tcatgttgca	cccttgtttc	tacacctgtg	240
ggttatgaca	aagacaactg	ccaaagaatc	ttcaagaagg	aggactgcaa	gtatatcgtg	300
gtggagaaga	aggacccaaa	aaagacctgt	tctgtcagtg	aatggataat	ctaattgtgct	360
tctagtaggc	acagggctcc	caggccaggc	ctcattctcc	tctggcctct	aatagtcaat	420
gattgtgtag	ccatgcctat	cagtaaaaag	atntttgagc	aaacacttt		469

<210> 165  
 <211> 195  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(195)  
 <223> n = A,T,C or G

<400> 165

acagtttttt	atanatatcg	acattgccgg	cacttgtgtt	cagtttcata	aagctgggtg	60
atccgctgtc	atccactatt	ccttggctag	agtaaaaatt	attcttatag	cccatgtccc	120
tgcaggccgc	ccgccgtag	ttctcgttcc	agtcgtcttg	gcacacaggg	tgccaggact	180
tctctgaga	tgagt					195

<210> 166  
 <211> 383  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(383)  
 <223> n = A,T,C or G

<400> 166

acatcttagt	agtgtggcac	atcagggggc	catcagggtc	acagtcactc	atagcctcgc	60
cgaggtcggg	gtccacacca	ccggtgtagg	tgtgctcaat	cttgggcttg	gcgccacact	120
ttggagaagg	gatatgctgc	acacacatgt	ccacaaagcc	tgtgaactcg	ccaaagaatt	180
tttgagacc	agcctgagca	aggggcggat	gttcagcttc	agctcctcct	tcgtcagggtg	240
gatgccaaac	tcgtctangg	tccgtgggaa	gctgggtgtc	acntcaccta	caacctgggc	300
gangatctta	taaagaggct	ccnagataaa	ctccacgaaa	cttctctggg	agctgctagt	360

nggggccttt ttggtgaact ttc

383

<210> 167  
 <211> 247  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(247)  
 <223> n = A,T,C or G

<400> 167  
 acagagccag accttggcca taaatgaanc agagattaag actaaacccc aagtccganat 60  
 tggagcagaa actggagcaa gaagtgggcc tggggctgaa gtagagacca aggccactgc 120  
 tatanccata cacagagcca actctcaggc caaggcnatg gttggggcag anccagagac 180  
 tcaatctgan tccaaagtgg tggctggaac actggtcatg acanaggcag tgactctgac 240  
 tgangtc 247

<210> 168  
 <211> 273  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(273)  
 <223> n = A,T,C or G

<400> 168  
 acttctaagt tttctagaag tggaaggatt gtantcatcc tgaaaatggg tttacttcaa 60  
 aatccctcan ccttggtctt cactactgtc tatactgana gtgtcatgtt tccacaaagg 120  
 gctgacacct gagcctgnat tttactcat ccctgagaag ccctttccag taggggtggc 180  
 aattcccaac ttccttgcca caagcttccc aggcctttctc ccctggaaaa ctccagcttg 240  
 agtcccagat acactcatgg gctgccctgg gca 273

<210> 169  
 <211> 431  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(431)  
 <223> n = A,T,C or G

<400> 169  
 acagccttgg cttccccaaa ctccacagtc tcagtgcaga aagatcatct tccagcagtc 60  
 agctcagacc aggggtcaaag gatgtgacat caacagtttc tggtttcaga acaggttcta 120  
 ctactgtcaa atgaccccc atacttcctc aaaggctgtg gtaagttttg cacaggtgag 180  
 ggcagcagaa aggggggtant tactgatgga caccatcttc tctgtatact ccacactgac 240  
 cttgccatgg gcaaaggccc ctaccacaaa aacaatagga tcactgctgg gcaccagctc 300  
 acgcacatca ctgacaaccg ggatggaaaa agaantgcc aactttcatac atccaactgg 360  
 aaagtgatct gatactggat tcttaattac cttcaaaagc ttctgggggc catcagctgc 420  
 tcgaacactg a 431

<210> 170  
 <211> 266  
 <212> DNA  
 <213> Homo sapien

<220>

<221> misc\_feature  
 <222> (1)...(266)  
 <223> n = A,T,C or G

<400> 170  
 acctgtgggc tgggctgtta tgcctgtgcc ggctgtgtaa agggagttca gaggtggagc 60  
 tcaaggagct ctgcaggcat ttgccaanc ctctccanag canagggagc aacctacact 120  
 ccccgctaga aagacaccag attggagtc tgggagggg agttgggtg ggcatttgat 180  
 gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg anattggcct 240  
 tcaaagctag ggtctggca ggtgga 266

<210> 171  
 <211> 1248  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(1248)  
 <223> n = A,T,C or G

<400> 171  
 ggcagccaaa tcataaacgg cgaggactgc agcccgact cgcagccctg gcaggcggca 60  
 ctggtcatgg aaaacgaatt gttctgctcg ggcgtcctgg tgcattccgca gtgggtgctg 120  
 tcagccgcac actgtttcca gaagtgagtg cagagctcct acaccatcgg gctgggcctg 180  
 cacagtcttg aggccgacca agagccaggg agccagatgg tggaggccag cctctccgta 240  
 cggcaccacg agtacaacag acccttgctc gctaaccgacc tcatgctcat caagttggac 300  
 gaatccgtgt ccgagctctga caccatccgg agcatcagca ttgcttcgca gtgccctacc 360  
 gcggggaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc 420  
 gtgctgcagt gcgtgaacgt gtcgggtggg tctgaggagg tctgcagtaa gctctatgac 480  
 ccgctgtacc accccagcat gttctgcgcc ggccggaggc aagaccagaa ggactcctgc 540  
 aacggtgact ctggggggcc cctgatctgc aacgggtact tgcagggcct tgtgtcttc 600  
 ggaaaagccc cgtgtggcca agttggcgtg ccagggtgtct acaccaacct ctgcaaattc 660  
 actgagtggga tagagaaaac cgtccaggcc agttaactct ggggactggg aacctatgaa 720  
 attgaccccc aaatacatcc tgcggaagga attcagggaat atctgttccc agcccctcct 780  
 cctcaggcc caggagtcca ggcgccagc ccctcctccc tcaaaccag ggtacagatc 840  
 ccagccctc cctccctcag acccaggagt ccagacccc cagccctcc tccctcagac 900  
 ccaggagtcc agcccctcct cctcagacc caggagtcca gacccccag cccctcctcc 960  
 ctgagacca ggggtccagg cccccaaccc ctccctcctc agactcagag gtccaagccc 1020  
 ccaaccntc attcccaga cccagaggtc cagggtcccag cccctcntcc ctgagacca 1080  
 gcggtccaat gccacctaga ctntccctgt acacagtgcc cccttggtgc acgttgaccc 1140  
 aaccttacca gttggttttt catTTTTngt ccctttcccc tagatccaga aataaagttt 1200  
 aagagaagng caaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 1248

<210> 172  
 <211> 159  
 <212> PRT  
 <213> Homo sapien

<220>  
 <221> VARIANT  
 <222> (1)...(159)  
 <223> Xaa = Any Amino Acid

<400> 172  
 Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro  
 1 5 10 15  
 Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser  
 20 25 30  
 Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr  
 35 40 45  
 Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly

50	55	60
Arg Met Pro Thr Val	Leu Gln Cys Val Asn Val	Ser Val Val Ser Glu
65	70	75
Glu Val Cys Ser Lys	Leu Tyr Asp Pro Leu Tyr	His Pro Ser Met Phe
85	90	95
Cys Ala Gly Gly Gln	Xaa Gln Xaa Asp Ser	Cys Asn Gly Asp Ser
100	105	110
Gly Gly Pro Leu Ile	Cys Asn Gly Tyr Leu Gln	Gly Leu Val Ser Phe
115	120	125
Gly Lys Ala Pro Cys	Gly Gln Val Gly Val Pro	Gly Val Tyr Thr Asn
130	135	140
Leu Cys Lys Phe Thr	Glu Trp Ile Glu Lys Thr	Val Gln Ala Ser
145	150	155

&lt;210&gt; 173

&lt;211&gt; 1265

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1)...(1265)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 173

ggcagcccg	actgcagcc	ctggcaggcg	gcactgggtca	tggaaaacga	attgttctgc	60
tcgggctcc	tggtgcatcc	gcagtgggtg	ctgtcagccg	cacactgttt	ccagaactcc	120
tacaccatcg	ggctgggctt	gcacagtctt	gagggcgacc	aagagccagg	gagccagatg	180
gtggaggcca	gcctctccgt	acggcaccca	gagtacaaca	gacccttgct	cgctaaccgac	240
ctcatgtcca	tcaagttaga	cgaatccgtg	tccgagtctg	acaccatccg	gagcatcagc	300
attgcttcgc	agtgccctac	cgcggggaac	tcttgccctg	tttctggctg	gggtctgctg	360
gcgaacggtg	agctcaaggg	tgtgtgtctg	ccctcttcaa	ggaggtcctc	tgcccagtcg	420
cgggggctga	cccagagctc	tgcgtcccag	gcagaatgcc	taccgtgctg	cagtgcgtga	480
acgtgtcggg	ggtgtctgag	gaggtctgca	gtaagctcta	tgacccgctg	taccacccca	540
gcatgttctg	cgccggcgga	gggcaagacc	agaaggactc	ctgcaacggt	gactctgggg	600
ggccccgat	ctgcaacggg	tacttgagg	gccttggtgc	tttcggaaaa	gccccgtgtg	660
gccaagttag	cgtgccagg	gtctacacca	acctctgcaa	attcactgag	tggatagaga	720
aaaccgtcca	ggccagttaa	ctctggggac	tgggaaaccca	tgaaattgac	ccccaataac	780
atcctgcgga	aggaattcag	gaatatctgt	tcccagcccc	tcctccctca	ggcccaggag	840
tccaggcccc	cagcccctcc	tccctcaaac	caagggtaca	gatccccagc	ccctcctccc	900
tcagaccag	gagtccagac	ccccagcccc	ctcctccctc	agacccagga	gtccagcccc	960
tcctcctcca	gaccaggag	tccagacccc	ccagcccctc	ctccctcaga	cccagggtt	1020
gaggccccca	accctcctc	cttcagagtc	agaggtccaa	gcccaccaac	cctcgttccc	1080
cagaccacaga	ggtnnaggtc	ccagcccctc	ttccntcaga	cccagnggtc	caatgccacc	1140
tagattttcc	ctgnacacag	tgcccccttg	tggnangttg	acccaacctt	accagttggt	1200
ttttcatttt	tngtcccttt	cccttagatc	cagaaataaa	gtttaagaga	ngngcaaaaa	1260
aaaaa						1265

&lt;210&gt; 174

&lt;211&gt; 1459

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1)...(1459)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 174

ggtcagccgc	acactgtttc	cagaagttag	tgagagctc	ctacaccatc	gggctgggcc	60
tgacagctct	tgaggccgac	caagagccag	ggagccagat	ggtaggggcc	agcctctccg	120
tacggcacc	agagtacaac	agacccttgc	tcgctaacga	cctcatgctc	atcaagttgg	180

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acgaatccgt gtccgagttct gacaccatcc ggagcatcag cattgcttcg cagtgcctta 240
ccgcggggaa ctcttgcttc gtttctggct ggggtctgct ggcgaacggt gagctcacgg 300
gtgtgtgtct gccctcttca aggaggctct ctgcccagtc gcgggggctg acccagagct 360
ctgcgtccca ggcagaatgc ctaccgtgct gcagtgcgtg aacgtgtcgg tgggtgtctga 420
ngaggtctgc antaagctct atgacccgct gtaccacccc ancatgttct gcgccggcgg 480
agggcaagac cagaaggact cctgcaacgt gagagagggg aaaggggagg gcaggcgact 540
caggaagggg tggagaaggg ggagacagag acacacaggg ccgcatggcg agatgcagag 600
atggagagac acacagggag acagtgacaa ctagagagag aaactgagag aaacagagaa 660
ataaacacag gaataaagag aagcaaagga agagagaaac agaaacagac atggggaggc 720
agaaacacac acacatagaa atgcagttga ctttccaaca gcatggggcc tgagggcggg 780
gacctccacc caatagaaaa tectcttata acttttgact ccccaaaaac ctgactagaa 840
atagcctact gttgacgggg agccttacca ataacataaa tagtcgattt atgcatacgt 900
tttatgcatt catgatatac ctttgttggg attttttgat atttctaagc tacacagttc 960
gtctgtgaat ttttttaaat tgttgcaact ctctaaaat ttttctgatg tgtttattga 1020
aaaaatccaa gtataagtgg acttgtgcat tcaaaccagg gttgttcaag ggtcaactgt 1080
gtaccacagag ggaacacagt acacagattc atagaggtga aacacgaaga gaaacaggaa 1140
aaatcaagac tctacaaaga ggctgggcag ggtggctcat gcctgtaatc ccagcacttt 1200
gggagggcag gcaggcgagat cacttgaggt aaggagttca agaccagcct ggccaaaatg 1260
gtgaaatcct gtctgtacta aaaatacaaa agttagctgg atatggtggc aggcgcctgt 1320
aatccagct acttgggagg ctgaggcagg agaattgctt gaatatggga ggcagaggtt 1380
gaagtgaagt gagatcacac cactatactc cagctggggc aacagagtaa gactctgtct 1440
caaaaaaaaa aaaaaaaaaa

```

```

<210> 175
<211> 1167
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(1167)
<223> n = A,T,C or G

```

```

<400> 175
gcgcagccct ggagggcgcc actgggtcatg gaaaacgaat tgttctgctc gggcgctcctg 60
gtgcatccgc agtgggtgct gtgagccgca cactgtttcc agaactccta caccatcggg 120
ctgggcctgc acagtcttga ggccgaccaa gagccaggga gccagatggt ggaggccagc 180
ctctccgtac ggcacccaga gtacaacaga ctcttgetcg ctaacgacct catgctcatc 240
aagtggagc aatccgtgtc cgagtctgac accatccgga gcatcagcat tgcctcgagc 300
tgccctaccg cggggaaactc ttgcctcgtn tctggctggg gtctgctggc gaacggcaga 360
atgcctaccg tgctgcaactg cgtgaacgtg tcggtgggtg ctgaggangt ctgcagtaag 420
ctctatgacc cgctgtacca cccagcatg ttctgcgccg gcggagggca agaccagaag 480
gactcctgca acggtgactc tggggggccc ctgatctgca acgggtactt gcagggcctt 540
gtgtctttcg gaaaagcccc gtgtggccaa cttggcgtgc caggtgtcta caccaacctc 600
tgcaaatcca ctgagtggtg agagaaaacc gtccagncca gtttaactctg gggactggga 660
acccatgaaa ttgacccccca aatacatcct gcggaangaa ttcagggaata tctgttccca 720
gcccctctc cctcaggccc aggagtccag gcccccagcc cctcctccct caaaccaagg 780
gtacagatcc ccagccctc ctccctcaga cccaggagtc cagaccccccc agcccctcnt 840
ccntcagacc caggagtcca gcccctctc cntcagacgc aggagtccag acccccagc 900
ccntcntccg tcagacccag ggtgacggc ccccaacccc tcntccntca gagtccagag 960
tccaagcccc caacccctcg ttccccagac ccagaggtnc aggtcccagc ccctcctccc 1020
tcagacccag cgggtccaatg ccacctagan tntccctgta cacagtgcc ccttgtggca 1080
ngttgaccca accttaccag ttggtttttc attttttgtc cctttcccct agatccagaa 1140
ataaagtnta agagaagcgc aaaaaaa

```

```

<210> 176
<211> 205
<212> PRT
<213> Homo sapien

```

```

<220>
<221> VARIANT

```

&lt;222&gt; (1)...(205)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 176

```

Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
1      5      10      15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
20      25      30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
35      40      45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Leu Leu Leu
50      55      60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
65      70      75      80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
85      90      95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met
100      105      110
Pro Thr Val Leu His Cys Val Asn Val Ser Val Val Ser Glu Xaa Val
115      120      125
Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala
130      135      140
Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly
145      150      155      160
Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys
165      170      175
Ala Pro Cys Gly Gln Leu Gly Val Pro Gly Val Tyr Thr Asn Leu Cys
180      185      190
Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Xaa Ser
195      200      205

```

&lt;210&gt; 177

&lt;211&gt; 1119

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 177

```

gcgcaactgc agccctggca ggcggcactg gtcattgaaa acgaattgtt ctgctcgggc      60
gtcctgggtgc atccgcagtg ggtgctgtca gccgcacact gtttccagaa ctctacacc      120
atcgggctgg gctgcacag tcttgaggcc gaccaagagc cagggagcca gatggtggag      180
gccagcctct ccgtacggca cccagagtac aacagaccct tgctcgctaa cgacctcatg      240
ctcatcaagt tggacgaatc cgtgtccgag tctgacacca tccggagcat cagcattgct      300
tcgcagtgcc ctaccgcggg gaactcttgc ctcgtttctg gctggggtct gctggcgaaac      360
gatgctgtga ttgccatcca gtcccagact gtgggaggct gggagtgtga gaagcttcc      420
caaccctggc aggttgttac catttcggca acttcagtg caaggacgtc ctgctgcac      480
ctcactgggt gctcactact gctcactgca tcacccggaa cactgtgatc aactagccag      540
caccatagtt ctccgaagtc agactatcat gattactgtg ttgactgtgc tgtctattgt      600
actaaccatg ccgatgttta ggtgaaatta gcgtcacttg gcctcaacca tcttggtatc      660
cagttatcct cactgaattg agatttctg cttcagtgtc agccattccc acataatttc      720
tgacctacag aggtgaggga tcatatagct cttcaaggat gctgggtactc ccctcacaaa      780
ttcatttctc ctggtgtagt gaaagggtgc ccctctggag cctcccaggg tgggtgtgca      840
ggtcacaatg atgaatgtat gatcgtgttc ccattaccca aagcctttaa atccctcatg      900
ctcagtacac cagggcaggt ctagcatttc ttcathtagt gtatgctgtc cattcatgca      960
accacctcag gactcctgga ttctctgcct agttgagctc ctgcatgctg cctccttggg      1020
gaggtgaggg agagggccca tggttcaatg ggatctgtgc agttgtaaca cattaggtgc      1080
ttaataaaca gaagctgtga tgtaaaaaaa aaaaaaaaaa      1119

```

&lt;210&gt; 178

&lt;211&gt; 164

&lt;212&gt; PRT

&lt;213&gt; Homo sapien



<220>  
 <221> VARIANT  
 <222> (1)...(164)  
 <223> Xaa = Any Amino Acid

<400> 178  
 Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp  
 1 5 10 15  
 Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu  
 20 25 30  
 Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val  
 35 40 45  
 Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu  
 50 55 60  
 Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser  
 65 70 75 80  
 Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly  
 85 90 95  
 Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val  
 100 105 110  
 Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu  
 115 120 125  
 Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg  
 130 135 140  
 Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Leu Thr Ala Ser  
 145 150 155 160  
 Pro Gly Thr Leu

<210> 179  
 <211> 250  
 <212> DNA  
 <213> Homo sapien

<400> 179  
 ctggagtgcc ttggtgtttc aagccccctgc aggaagcaga atgcaccttc tgaggcacct 60  
 ccagctgccc ccggccgggg gatgcgaggc tcggagcacc cttgcccggc tgtgattgct 120  
 gccaggcaact gttcatctca gcttttctgt ccctttgctc ccggcaagcg cttctgctga 180  
 aagttcatat ctggagcctg atgtcttaac gaataaaggt cccatgctcc acccgaaaaa 240  
 aaaaaaaaaa 250

<210> 180  
 <211> 202  
 <212> DNA  
 <213> Homo sapien

<400> 180  
 actagtccag tgtggtggaa ttccattgtg ttgggcccaa cacaatggct acctttaaca 60  
 tcacccagac ccgcccctg ccgctgcccc acgctgctgc taacgacagt atgatgctta 120  
 ctctgctact cggaaactat ttttatgtaa ttaatgtatg ctttctgtt tataaatgcc 180  
 tgatttaaaa aaaaaaaaaa aa 202

<210> 181  
 <211> 558  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(558)  
 <223> n = A,T,C or G

```

<400> 181
tccytttgkt naggtttkkg agacamccck agacctwaan ctgtgtcaca gacttcynng 60
aatgttttagg cagtgcctagt aatttctytcg taatgattct gttattactt tcctnattct 120
ttattcctct ttcttctgaa gattaatgaa gttgaaaatt gaggtggata aatacaaaaa 180
ggtagtgtga tagtataagt atctaagtgc agatgaaagt gtgttatata tatccattca 240
aaattatgca agttagtaat tactcagggt taactaaatt actttaatat gctgttgaaac 300
ctactctgtt ccttggctag aaaaaattat aaacaggact ttgttagttt gggaagccaa 360
attgataata ttctatgttc taaaagttgg gctatacata aattattaag aaatatggaw 420
ttttattccc aggaatatgg kgttcatttt atgaatatta cscrggatag awgtwtgagt 480
aaaaycagtt ttggtwaata ygtwaatatg tcmtaaataa acaakgcttt gacttatttc 540
caaaaaaaaa aaaaaaaaa 558

```

```

<210> 182
<211> 479
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(479)
<223> n = A,T,C or G

```

```

<400> 182
acagggwttk grggatgcta agsccccrga rwtggtttga tccaaccctg gcttwttttc 60
agaggggaaa atggggccta gaagttacag mscatytagy tgggtgcgmg gcacccctgg 120
cstcacacag astcccgagt agctgggact acaggcacac agtcactgaa gcaggccctg 180
ttwgcaattc acgttgccac ctccaactta aacattcttc atatgtgatg tccttagtca 240
ctaagggttaa actttccac ccagaaaagg caacttagat aaaatcctag agtactttca 300
tactmttcta agtcctcttc cagcctcact kkgagtctm cytgggggtt gataggaant 360
ntctcttggc tttctcaata aartctctat ycatctcatg ttttaatttg tacgcatara 420
awtgstgara aaattaaaat gttctggtty mactttaaaa aaaaaaaaaa aaaaaaaaaa 479

```

```

<210> 183
<211> 384
<212> DNA
<213> Homo sapien

```

```

<400> 183
aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc 60
agtaccagta ccaataacag tgccagtgcc agtgccagca ccagtgggtg cttcagtgtc 120
ggtgccagcc tgaccgccac tctcacattt gggctcttcg ctggccttgg tggagctggt 180
gccagcacca gtggcagctc tgggtgctgt gggttctcct acaagtgaga ttttagatat 240
tgttaatcct gccagctctt ctcttcaagc caggggtgcat cctcagaaac ctactcaaca 300
cagcactcta ggcagccact atcaatcaat tgaagttgac actctgcatt aratctattt 360
gccatttcaa aaaaaaaaaa aaaa 384

```

```

<210> 184
<211> 496
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(496)
<223> n = A,T,C or G

```

```

<400> 184
accgaattgg gaccgtggc ttataagcga tcatgtyynt ccrgtatkac ctcaacgagc 60
aggagatcg agtctatacg ctgaagaaat ttgacccgat gggacaacag acctgctcag 120
cccctcctgc tcggttctcc ccagatgaca aatactctsg acaccgaatc accatcaaga 180
aacgcttcaa ggtgctcatg acccagcaac cgcgccctgt cctctgaggg tcccttaaac 240
tgatgtcttt tctgcacact gttaccctc ggagactccg taaccaaact cttcgactg 300

```

tgagccctga	tgcctttttg	ccagccatac	tctttggcat	ccagtctctc	gtggcgattg	360
attatgcttg	tgtgaggcaa	tcatggtggc	atcaccata	aagggaacac	atttgacttt	420
tttttctcat	attttaaatt	actacmagaw	tattwmagaw	waaatgawtt	gaaaaactst	480
taaaaaaaaa	aaaaaa					496

<210> 185  
 <211> 384  
 <212> DNA  
 <213> Homo sapien

<400> 185						
gctggtagcc	tatggcgkkg	cccacggagg	ggctcctgag	gccacggrac	agtgacttcc	60
caagtatcyt	gcgscgctc	ttctaccgtc	cctacctgca	gatcttcggg	cagattcccc	120
aggaggacat	ggacgtggcc	ctcatggagc	acagcaactg	yticgtcggag	cccggcttct	180
gggcacaccc	tcctggggcc	caggcgggca	cctgcgtctc	ccagtatgcc	aactggctgg	240
tgggtctgct	cctcgctcatc	ttcctgctcg	tggccaacat	cctgctggtc	aacttgctca	300
ttgccatggt	cagttacaca	ttcggcaaag	tacagggcaa	cagcgatctc	tactgggaag	360
gcgcagcgtt	accgcctcat	ccgg				384

<210> 186  
 <211> 577  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(577)  
 <223> n = A,T,C or G

<400> 186						
gagttagctc	ctccacaacc	ttgatgaggt	cgtctgcagt	ggcctctcgc	ttcataccgc	60
tnccatcgctc	atactgtagg	tttgccacca	cytcctggca	tcttggggcg	gcntaatatt	120
ccaggaaact	gtcaatcaag	tcaccgtcga	tgaaacctgt	gggctgggtc	tgtcttccgc	180
tcggtgtgaa	aggatctccc	agaaggagtg	ctcgatcttc	cccacacttt	tgatgacttt	240
attgagtcga	ttctgcatgt	ccagcaggag	gttgtaccag	ctctctgaca	gtgaggtcac	300
cagccctatc	atgccgttga	mcgtgccgaa	garcaccgag	ccttgtgtgg	gggkkgaaat	360
ctcaccacaga	ttctgcatta	ccagagagcc	gtggcaaaaag	acattgacaa	actcgcccag	420
gtggaaaaag	amcamctcct	ggargtgctn	gccgtctctc	gtcmgttggt	ggcagcgctw	480
tccttttgac	acacaaaaca	gttaaaggca	ttttcagccc	ccagaaaantt	gtcatcatcc	540
aagatntcgc	acagcactna	tccagttggg	attaaat			577

<210> 187  
 <211> 534  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(534)  
 <223> n = A,T,C or G

<400> 187						
aacatcttcc	tgtataatgc	tgtgtaatat	cgatccgatn	ttgtctgstg	agaatycatw	60
actkggaaaa	gmaacattaa	agcctggaca	ctggtattaa	aattcacaaat	atgcaacact	120
ttaaacagtg	tgtcaatctg	ctcccyynac	tttgtcatca	ccagtctggg	aakaagggtg	180
tgccctattc	acacctgtta	aaagggcgct	aagcattttt	gattcaacat	cttttttttt	240
gacacaagtc	cgaaaaaagc	aaaagtaaac	agttatyaat	ttgttagcca	attcactttc	300
ttcatgggac	agagccatyt	gatttaaaaa	gcaaattgca	taatattgag	cttygggagc	360
tgatatttga	gcggaagagt	agcctttcta	cttcaccaga	cacaactccc	tttcatattg	420
ggatgttnac	naaagtwatg	tctctwacag	atgggatgct	tttgtggcaa	ttctgttctg	480
aggatctccc	agtttattta	ccacttgcac	aagaaggcgt	tttcttctc	aggc	534

<210> 188  
 <211> 761  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(761)  
 <223> n = A,T,C or G

<400> 188  
 agaaaccagt atctctnaaa acaacctctc ataccttgtg gacctaatth tgtgtgcgtg 60  
 tgtgtgtgcg cgcataattat atagacaggc acatcttttt tacttttgta aaagcttatg 120  
 cctcttttgt atctatatct gtgaaagtth taatgatctg ccataatgtc ttgggggacct 180  
 ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcaa tctagttngt 240  
 ttatttcgac atgaaggaaa tttccagatn acaacactna caaactctcc ctkgackarg 300  
 ggggacaaaag aaaagcaaaa ctgamcataa raaacaatwa cctggtgaga arttgcataa 360  
 acagaaatwr ggtagtatat tgaarnacag catcattaaa rmgttwktt wtctccctt 420  
 gcaaaaaaca tgtacngact tcccgttgag taatgccaag ttgttttttt tatnataaaa 480  
 cttgcccttc attacatggt tnaaagtggg gtggtggggc aaaatattga aatgatggaa 540  
 ctgactgata aagctgtaca aataagcagt gtgcctaaca agcaacacag taatgttgac 600  
 atgcttaatt cacaaatgct aatttcatta taaatgtttg ctaaaataca ctttgaacta 660  
 tttttctgtn ttccagagc tgagatntta gattttatgt agtatnaagt gaaaaantac 720  
 gaaaataata acattgaaga aaaaananaa aaanaaaaaa a 761

<210> 189  
 <211> 482  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(482)  
 <223> n = A,T,C or G

<400> 189  
 tttttttttt ttgtccgatn ctactattht attgeaggan gtgggggtgt atgcaccgca 60  
 caccggggct atnagaagca agaagggaagg agggagggca cagccccttg ctgagcaaca 120  
 aagccgcctg ctgccttctc tgtctgtctc ctggtgcagg cacatgggga gaccttcccc 180  
 aaggcagggg ccaccagtcc aggggtggga atacaggggg tgggagtgt gcataagaag 240  
 tgataggcac aggcaccccg gtacagaccc ctgcgctcct gacaggtnga tttcgaccag 300  
 gtcattgtgc cctgcccagg cacagcgtn atctggaaaa gacagaatgc tttccttttc 360  
 aaatttggt ngtcatngaa ngggcanttt tccaantng gctnggtctt ggtacnctg 420  
 gttcggccca gtcncngtc caaaaantat tcaccennct ccnaattgct tgcngnccc 480  
 cc 482

<210> 190  
 <211> 471  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(471)  
 <223> n = A,T,C or G

<400> 190  
 tttttttttt ttttaaaaca gtttttcaca aaaaaattta ttagaagaat agtggttttg 60  
 aaaactctcg catccagtga gaactacat acaccacatt acagctngga atgtntcca 120  
 aatgtctggt caaatgatac aatggaacca ttcaatctta cacatgcag aaagaacaag 180  
 cgcttttgac atacaatgca caaaaaaaaa aggggggggg gaccacatgg attaaaaatt 240  
 taagtactca tcacatacat taagacacag ttctagtcca gtcnaaaatc agaactgcnt 300

```

tgaaaaattt catgtatgca atccaaccaa agaacttnat tggatgatcat gantncteta 360
ctacatcnac cttgatcatt gccaggaacn aaaagttnaa ancacncngt acaaaaaanaa 420
tctgtaattn anttcaacct ccgtacngaa aaatntntnt tatacactcc c 471

```

```

<210> 191
<211> 402
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(402)
<223> n = A,T,C or G

```

```

<400> 191
gagggattga aggtctgttc tastgtcggm ctgttcagcc accaactcta acaagttgct 60
gtcttccact cactgtctgt aagcttttta acccagacwg tatcttcata aatagaacaa 120
attcttcacc agtcacatct tctaggacct ttttgattc agttagtata agctcttcca 180
cttcctttgt taagacttca tctggtaaag tcttaagttt tgtagaaagg aattyaattg 240
ctcgttctct aacaatgtcc tctccttgaa gtatttggct gaacaacca cctaaagtcc 300
ctttgtgcat ccattttaaa tatacttaat agggcattgk tncactaggt taaattctgc 360
aagagtcata tgtctgcaaa agttgcgtta gtatatctgc ca 402

```

```

<210> 192
<211> 601
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(601)
<223> n = A,T,C or G

```

```

<400> 192
gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact 60
ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtccagc 120
atgcytyttt gaytaccgtg tgccaagtgc tggatgattc yaacacacyt ccatcccggt 180
cttttgtaga aaaactggca cttktctgga actagcarga catcacttac aaattcaccc 240
acgagacact tgaaaagggt aacaaaagcga ytcttgcat gctttttgtc cctccggcac 300
cagttgtcaa tactaaccgg ctggtttgcc tccatcacat ttgtgatctg tagctctgga 360
tacatctcct gacagtactg aagaacttct tcttttggtt caaaagcarg tcttggtgcc 420
tgttggatca gggtccatt tcccagtcyg aatgttcaca tggcatattt wacttccac 480
aaaacattgc gatttgaggc tcagcaacag caaatcctgt tccggcattg gctgcaagag 540
cctcgatgta gccggccagc gccaaaggcag gcgccgtgag ccccaccagc agcagaagca 600
g 601

```

```

<210> 193
<211> 608
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(608)
<223> n = A,T,C or G

```

```

<400> 193
atacagccca natcccacca cgaagatgcg ctgttgact gagaacctga tgcggtcact 60
gggtcccgctg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcytt 120
cccaacgcag gcagmagcgg gscgggtcaa tgaactccay tcgtggcttg gggtkgacgg 180
tkaagtgcag gaagaggctg accacctcgc ggtccaccag gatgcccgac tgtgcgggac 240
ctgcagcgaa actcctcgat ggtcatgagc ggaagcgaa tgaggcccag ggccttgccc 300

```

agaaccttcc	gcctgttctc	tggcgtcacc	tgcagctgct	gccgctgaca	ctcggcctcg	360
gaccagcgga	caaacggcrt	tgaacagccg	cacctcacgg	atgccacgtg	tgctcgcgctc	420
caggammgsc	accagcgtgt	ccagggtcaat	gtcgggtgaag	ccctccgcgg	gtrattggcgt	480
ctgcagtggt	tttgtcgatg	ttctccaggc	acaggctggc	cagctgcggt	tcattcgaaga	540
gtcgcgcctg	cgtaggcagc	atgaaggcgt	tgctggctcg	cagttcttct	tcagggaactc	600
cacgcaat						608

<210> 194  
 <211> 392  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(392)  
 <223> n = A,T,C or G

<400> 194						
gaacggctgg	accttgccctc	gcattgtgct	tgctggcagg	gaataccttg	gcaagcagyt	60
ccagtccgag	cagccccaga	ccgctgccgc	ccgaagctaa	gcctgcctct	ggccttcccc	120
tccgcctcaa	tgagaacca	gtagtgggag	caatgtgttt	agagttaaga	gtgaacactg	180
tttgatttta	cttggaatt	tcctctgtta	tatagctttt	cccaatgcta	atttccaaac	240
aacaacaaca	aaataacatg	tttgccctgtt	aagttgtata	aaagtaggtg	attctgtatt	300
taaagaaaaa	attactgtta	catatactgc	ttgcaatttc	tgtatttatt	gktnctstgg	360
aaataaatat	agttattaaa	ggttgtcant	cc			392

<210> 195  
 <211> 502  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(502)  
 <223> n = A,T,C or G

<400> 195						
ccsttkgagg	ggtkaggkyc	cagtttyccga	gtggaagaaa	caggccagga	gaagtgcgtg	60
ccgagctgag	gcagatgttc	ccacagtgcg	ccccagagcc	stgggstata	gtytctgacc	120
cctcncaagg	aaagaccacs	ttctggggac	atgggctgga	gggcaggacc	tagaggcacc	180
aagggaaggc	ccattccgg	ggstgttccc	cgaggaggaa	gggaaggggc	tctgtgtgcc	240
ccccasgagg	aagaggccct	gagtcctggg	atcagacacc	ccttcacgtg	tatccccaca	300
caaatgcaag	ctcaccaagg	tcccccttca	gtccccttcc	stacaccctg	amcgccact	360
gscscacacc	caccagagc	acgccacccg	ccatggggar	tgtgtcgaag	gartcgcnng	420
gcarcgtgga	catctngtcc	cagaaggggg	cagaatctcc	aatagangga	ctgarcmstt	480
gctnanaaaa	aaaaanaaaa	aa				502

<210> 196  
 <211> 665  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(665)  
 <223> n = A,T,C or G

<400> 196						
ggttacttgg	tttcattgcc	accacttagt	ggatgtcatt	tagaaccatt	ttgtctgctc	60
cctctggaag	ccttgccgag	agcggacttt	gtaattgttg	gagaataact	gctgaatttt	120
wagctgtttk	gagttgatts	gcaccactgc	acccacaact	tcaatatgaa	aacyawttga	180
actwatttat	tatcttgtga	aaagtataac	aatgaaaatt	ttgttcatac	tgtattkatc	240

```

aagtatgatg aaaagcaawa gatatatatt cttttattat gttaaattat gattgccatt 300
attaatcggc aaaatgtgga gtgtatgttc ttttcacagt aatatatgcc ttttgaact 360
tcacttggtt attttattgt aaatgartta caaaattctt aatttaagar aatggtagt 420
watatttatt tcattaattt ctttcctkgt ttacgtwaat tttgaaaaga wtgcatgatt 480
tcttgacaga aatcgatctt gatgctgtgg aagtagtttg acccacatcc ctatgagttt 540
ttcttagaat gtataaagggt tgtagcccat cnaacttcaa agaaaaaaat gaccacatac 600
tttgcaatca ggctgaaatg tggcatgctn ttctaattcc aactttataa actagcaaan 660
aagtg 665

```

```

<210> 197
<211> 492
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(492)
<223> n = A,T,C or G

```

```

<400> 197
tttntttttt ttttttttgc aggaaggatt ccattttattg tggatgcatt ttcacaatat 60
atgtttattg gagcgatcca ttatcagtga aaagtatcaa gtgtttataa natttttagg 120
aaggcagatt cacagaacat gctngtcngc ttgcagtttt acctcgtana gatnacagag 180
aatttatagtc naaccagtaa acnaggaatt tacttttcaa aagattaaat ccaaactgaa 240
caaaattcta ccctgaaact tactccatcc aaatattgga ataanagtca gcagtgtac 300
attctcttct gaacttttaga ttttctagaa aaatatgtaa tagtgatcag gaagagctct 360
tgttcaaaag tacaacnaag caatgttccc ttaccatagg ccttaattca aactttgatc 420
catttcactc ccattcacggg agtcaatgct acctgggaca cttgtatttt gttcatnctg 480
ancntggctt aa 492

```

```

<210> 198
<211> 478
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(478)
<223> n = A,T,C or G

```

```

<400> 198
tttnttttgn atttcantct gtannaanta ttttcattat gtttattana aaaatatnaa 60
tgtntccacn acaaatcatn ttacntnagt aagaggccan ctacattgta caacatacac 120
tgagtatatt ttgaaaagga caagtttaaa gtanacncat attgccganc atancacatt 180
tatacatggc ttgattgata tttagcacag canaaactga gtgagttacc agaaaanaat 240
natatatgtc aatcngattt aagatacaaa acagatccta tggtagatan catcntgtag 300
gagttgtggc tttatgttta ctgaaagtca atgcagttcc tgtacaaaga gatggccgta 360
agcattctag tacctctact ccatggttaa gaatcgta cttatgttta catatgtnca 420
gggtaagaat tgtgttaagt naanttatgg agaggtccan gagaaaaatt tgatncaa 478

```

```

<210> 199
<211> 482
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(482)
<223> n = A,T,C or G

```

```

<400> 199
agtgacttgt cctccaacaa aacccttga tcaagtttgt ggactgaca atcagaccta 60

```

tgctagttcc	tgatcatctat	tcgctactaa	atgcagactg	gaggggacca	aaaaggggca	120
tcaactccag	ctggattatt	ttggagcctg	caaactctatt	cctacttgta	cggactttga	180
agtgattcag	tttcctctac	ggatgagaga	ctgggtcaag	aatatcctca	tgacagcttta	240
tgaagccnac	tctgaacacg	ctggttatct	nagatgagaa	ncagagaaat	aaagtcnaga	300
aaatttacct	ggangaaaag	aggctttngg	ctggggacca	tcccattgaa	ccttctctta	360
anggacttta	agaanaaact	accacatgtn	tgtngtatcc	tggtgccngg	ccgtttantg	420
aacntngacn	ncacccttnt	ggaatanant	cttgacngcn	tcctgaactt	gctcctctgc	480
ga						482

&lt;210&gt; 200

&lt;211&gt; 270

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(270)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 200

cggccgcaag	tgcaactcca	gctggggccg	tgccggacgaa	gattctgccca	gcagttgggtc	60
cgactgcgac	gacggcggcg	gcgacagtcg	caggtgcagc	gcggggcgcc	gggtcttgc	120
aaggctgagc	tgacgccgca	gaggtcgtgt	cacgtcccac	gaccttgacg	ccgtcgggga	180
cagccggaac	agagcccggt	gaangcggga	ggcctcgggg	agcccctcgg	gaagggcgcg	240
ccgagagata	cgcaggtgca	ggtggccgccc				270

&lt;210&gt; 201

&lt;211&gt; 419

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(419)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 201

tttttttttt	tttttgaatc	tactgcgagc	acagcaggtc	agcaacaagt	ttatttttgc	60
gctagcaagg	taacagggta	gggcatgggt	acatgttcag	gtcaacttcc	tttgctgtgg	120
ttgattgggt	tgtctttatg	ggggcggggg	ggggtagggg	aaancgaagc	anaantaaca	180
tgagtggggt	gcacctctcc	tgtagaacct	ggttacnaaa	gcttggggca	gttcacctgg	240
tctgtgaccg	tcattttctt	gacatcaatg	ttattagaag	tcaggatatc	ttttagagag	300
tccactgtnt	ctggagggag	attagggttt	cttgccaana	tccaancaaa	atccacntga	360
aaaagtgtga	tgatncangt	acngaatacc	ganggcatan	ttctcatant	cgggtggcca	419

&lt;210&gt; 202

&lt;211&gt; 509

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(509)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 202

tttttttttt	tttttttttt	tttttttttt	tttttttttt	tttttttttt	tttttttttt	60
tggcacttaa	tccattttta	tttcaaaatg	tctacaaant	ttnaatncnc	cattatacng	120
gtnattttnc	aaaatctaaa	nnttattcaa	atntnagcca	aantccttac	ncaaatnnaa	180
tacnncnaaa	aatcaaaaat	atacntntct	ttcagcaaac	ttngttacat	aaattaaaaa	240
aatatatacg	gctggtgttt	tcaaagtaca	attatcttaa	cactgcaaac	atnttttnaa	300
ggaactaaaa	taaaaaaaa	cactnccgca	aaggttaaag	ggaacaacaa	attcntttta	360



```
<210> 203
<211> 583
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(583)
<223> n = A,T,C or G
```

```
<210> 204
<211> 589
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(589)
<223> n = A,T,C or G
```

```
<210> 205
<211> 545
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(545)
<223> n = A,T,C or G
```

<400> 205						
ttttntttt	tttttcagt	aataatcaga	acaatattta	tttttatatt	taaaattcat	60
agaaaagtgc	cttacattta	ataaaagttt	gtttctcaaa	gtgatcagag	gaattagata	120
tngtcttgaa	caccaatatt	aatttgagga	aaatacacca	aaatacatta	agtaaattat	180

ttaagatcat	agagcttgta	agtgaaaaga	taaaatttga	cctcagaaac	tctgagcatt	240
aaaaatccac	tattagcaaa	taaattacta	tggacttctt	gctttaattt	tgtgatgaat	300
atgggggtg	actggtaaac	caacacattc	tgaaggatac	attacttagt	gatagattct	360
tatgtacttt	gctanatnac	gtggatatga	gttgacaagt	ttctctttct	tcaatctttt	420
aaggggcnga	ngaaatgagg	aagaaaagaa	aaggattacg	catactgttc	tttctatngg	480
aaggattaga	tatgtttcct	ttgccaatat	taaaaaaata	ataatgttta	ctactagtga	540
aaccc						545

<210> 206  
 <211> 487  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(487)  
 <223> n = A,T,C or G

<400> 206						
tttttttttt	tttttttagtc	aagtttctna	tttttattat	aattaaagtc	ttggtcattt	60
catttattag	ctctgcaact	tacatattta	aattaaagaa	acgttnttag	acaactgtna	120
caatttataa	atgtaagggtg	ccattattga	gtanatata	tcctccaaga	gtggatgtgt	180
cccttctccc	accaactaat	gaancagcaa	cattagttta	attttattag	tagatnatac	240
actgctgcaa	gcgctaattc	tcttctccat	ccccatgtng	atattgtgta	tatgtgtgag	300
ttggtanagaa	tgcatacanca	atctnacaat	caacagcaag	atgaagctag	gcntgggctt	360
tcggtgaaaa	tagactgtgt	ctgtctgaat	caaagtatct	gacctatcct	cgggtggcaag	420
aactcttcga	accgcttcct	caaaggcngc	tgccacattt	gtggcntctn	ttgcacttgt	480
ttcaaaa						487

<210> 207  
 <211> 332  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(332)  
 <223> n = A,T,C or G

<400> 207						
tgaattggct	aaaagactgc	atttttanaa	ctagcaactc	ttatttcttt	cctttaaaaa	60
tacatagcat	taaatcccaa	atcctattta	aagacctgac	agcttgagaa	ggtcactact	120
gcatttatag	gaccttctgg	tggttctgct	gttacntttg	aantctgaca	atccttgana	180
atctttgcat	gcagaggagg	taaaagggtat	tggattttca	cagaggaana	acacagcgca	240
gaaatgaagg	ggccaggcct	actgagcttg	tccactggag	ggctcatggg	tgggacatgg	300
aaaagaaggc	agcctaggcc	ctggggagcc	ca			332

<210> 208  
 <211> 524  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(524)  
 <223> n = A,T,C or G

<400> 208						
agggcggtgt	gcggaggcg	ttactgtttt	gtctcagtaa	caataaatac	aaaaagactg	60
gttgtgttcc	ggccccatcc	aaccacgaag	ttgatttctc	ttgtgtgcag	agtgactgat	120
tttaaggac	atggagcttg	tcacaatgtc	acaatgtcac	agtgtgaagg	gcacactcac	180
tccgcggtga	ttcacattta	gcaaccaaca	atagctcatg	agtccatact	tgtaaatact	240

tttggcagaa tacttnttga aacttgcaga.tgataactaa gatccaagat atttcccaa	300
gtaaatagaa gtgggtcata atattaatta cctgttcaca tcagcttcca tttacaagtc	360
atgagcccag aactgacat caaactaagc ccacttagac tcctcaccac cagtctgtcc	420
tgatcatcaga caggaggctg tcaccttgac caaattctca ccagtcaatc atctatccaa	480
aaaccattac ctgatccact tccggtaatg caccaccttg gtga	524

<210> 209  
 <211> 159  
 <212> DNA  
 <213> Homo sapien

<400> 209	
gggtgaggaa atccagagtt gccatggaga aaattccagt gtcagcattc ttgctccttg	60
tggccctctc ctacactctg gccagagata ccacagtcaa acctggagcc aaaaaggaca	120
caaaggactc tcgacccaaa ctgcccacaga ccctctcca	159

<210> 210  
 <211> 256  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(256)  
 <223> n = A,T,C or G

<400> 210	
actccctggc agacaaaggc agaggagaga gctctgttag ttctgtgttg ttgaactgcc	60
actgaatttc ttccacttg gactattaca tgccanttga gggactaatg gaaaaacgta	120
tggggagatt ttanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat	180
ttgcagggtg naaatgggan ggctggtttg ttanatgaac agggacatag gaggtaggca	240
ccaggatgct aatatca	256

<210> 211  
 <211> 264  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(264)  
 <223> n = A,T,C or G

<400> 211	
acattgtttt tttagataaa agcattgaga gagctctcct taacgtgaca caatggaagg	60
actggaacac ataccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt	120
atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gttaaggaga	180
ggggagatac attcngaaag aggactgaaa gaaatactca agtnggaaaa cagaaaaaga	240
aaaaaaggag caaatgagaa gcct	264

<210> 212  
 <211> 328  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(328)  
 <223> n = A,T,C or G

<400> 212	
acccaaaaat ccaatgctga atatttggct tcattattcc canattcttt gattgtcaaa	60

ggattttaatg	ttgtctcagc	ttgggcactt	cagttaggac	ctaaggatgc	cagccggcag	120
gtttatatat	gcagcaacaa	tattcaagcg	cgacaacagg	ttattgaact	tgcccggcag	180
ttnaatttca	ttccattga	cttgggatcc	ttatcatcag	ccagagagat	tgaaaattta	240
ccccacnac	tctttactct	ctgganaggg	ccagtgggtg	tagctataag	cttggccaca	300
tttttttttc	ctttattcct	ttgtcaga				328

<210> 213  
 <211> 250  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(250)  
 <223> n = A,T,C or G

<400> 213						
acttatgagc	agagcgacat	atccnagtgt	agactgaata	aaactgaatt	ctctccagtt	60
taaagcattg	ctcactgaag	ggatagaagt	gactgccagg	agggaaaagta	agccaaggct	120
cattatgccca	aagganatat	acattttcaat	tctccaaact	tcttcctcat	tccaagagtt	180
ttcaatattt	gcatgaacct	gctgataanc	catgttaana	aacaaatata	tctctnacct	240
tctcatcggt						250

<210> 214  
 <211> 444  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(444)  
 <223> n = A,T,C or G

<400> 214						
accagaatc	caatgctgaa	tatttggtt	cattattccc	agattctttg	attgtcaaag	60
gattttaatg	tgtctcagct	tgggcacttc	agttaggacc	taaggatgcc	agccggcagg	120
tttatatatg	cagcaacaat	attcaagcgc	gacaacagg	tattgaactt	gcccggcag	180
tgaatttcac	tcccattgac	ttgggatcct	tatcatcagc	canagagatt	gaaaatttac	240
ccctacgact	ctttactctc	tggagagggc	cagtgggtgt	agctataaag	ttggccacat	300
ttttttttcc	tttattcctt	tgtcagagat	gcgattcatc	catatgctan	aaaccaacag	360
agtgaacttt	acaaaattcc	tataganatt	gtgaataaaa	ccttacctat	agttgccatt	420
actttgctct	ccctaataata	cctc				444

<210> 215  
 <211> 366  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(366)  
 <223> n = A,T,C or G

<400> 215						
acttatgagc	agagcgacat	atccaagtgt	anactgaata	aaactgaatt	ctctccagtt	60
taaagcattg	ctcactgaag	ggatagaagt	gactgccagg	agggaaaagta	agccaaggct	120
cattatgccca	aagganatat	acattttcaat	tctccaaact	tcttcctcat	tccaagagtt	180
ttcaatattt	gcatgaacct	gctgataagc	catgttgaga	aacaaatata	tctctgacct	240
tctcatcggt	aagcagaggc	tgtaggcaac	atggaccata	gcgaanaaaa	aacttagtaa	300
tccaagctgt	tttctacact	gtaaccaggt	ttccaaccaa	ggtggaaatc	tcctatactt	360
ggtgcc						366

<210> 216  
 <211> 260  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(260)  
 <223> n = A,T,C or G

<400> 216  
 ctgtataaac agaactccac tgcangaggg agggccgggc caggagaatc tccgcttgtc 60  
 caagacaggg gcctaaggag ggtctccaca ctgctnntaa gggctnttnc atttttttat 120  
 taataaaaag tnnaaaaggc ctcttctcaa cttttttccc ttnggctgga aaatttaaaa 180  
 atcaaaaatt tcctnaagtt ntcaagctat catatatact ntatcctgaa aaagcaacat 240  
 aattcttctt tccctccttt 260

<210> 217  
 <211> 262  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(262)  
 <223> n = A,T,C or G

<400> 217  
 acctacgtgg gtaagtttan aaatgttata atttcaggaa naggaacgca tataattgta 60  
 tcttgccctat aattttctat ttaataaagg aaatagcaaa ttgggggtggg gggaatgtag 120  
 ggcattctac agtttgagca aaatgcaatt aaatgtggaa ggacagcact gaaaaatttt 180  
 atgaataatc tgtatgatta tatgtctcta gagtagattt ataattagcc acttaccta 240  
 atatccttca tgcttgtaaa gt 262

<210> 218  
 <211> 205  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(205)  
 <223> n = A,T,C or G

<400> 218  
 accaaggtgg tgcattaccg gaantggatc aangacacca tcgtggccaa cccctgagca 60  
 cccctatcaa ctcccttttg tagtaaaactt ggaaccttgg aaatgaccag gccaaagactc 120  
 aggcctcccc agttctactg acctttgtcc ttangtnna ngtccagggt tgctaggaaa 180  
 anaaatcagc agacacaggt gtaaa 205

<210> 219  
 <211> 114  
 <212> DNA  
 <213> Homo sapien

<400> 219  
 tactgttttg tctcagtaac aataaatata aaaagactgg ttgtgttccg gccccatcca 60  
 accacgaagt tgatttctct tgtgtgcaga gtgactgatt ttaaaggaca tgga 114

<210> 220  
 <211> 93  
 <212> DNA

<213> Homo sapien

<400> 220

actagccagc	acaaaaggca	gggtagcctg	aattgctttc	tgctctttac	atttctttta	60
aaataagcat	ttagtgctca	gtccctactg	agt			93

<210> 221

<211> 167

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(167)

<223> n = A,T,C or G

<400> 221

actangtgca	ggtgcgcaca	aatatttgtc	gatattccct	tcatcttgga	ttccatgagg	60
tcttttgccc	agcctgtggc	tctactgtag	taagtttctg	ctgatgagga	gccagnatgc	120
ccccactac	cttccctgac	gctcccccana	aatcacccaa	cctctgt		167

<210> 222

<211> 351

<212> DNA

<213> Homo sapien

<400> 222

agggcgtggt	gcgaggggcg	gtactgacct	cattagtagg	aggatgcatt	ctggcacccc	60
gttcttcacc	tgcccccaa	tccttaaaaag	gccatactgc	ataaagtcaa	caacagataa	120
atgtttgctg	aattaaagga	tggatgaaaa	aaattaataa	tgaatttttg	cataatccaa	180
ttttctcttt	tatatttcta	gaagaagttt	ctttgagcct	attagatccc	gggaatcttt	240
taggtgagca	tgattagaga	gcttgtaggt	tgcttttaca	tatatctggc	atatttgagt	300
ctcgtatcaa	aacaatagat	tggtaaaggt	ggtattattg	tattgataag	t	351

<210> 223

<211> 383

<212> DNA

<213> Homo sapien

<220>

<221> misc\_feature

<222> (1)...(383)

<223> n = A,T,C or G

<400> 223

aaaacaaaca	aacaaaaaaa	acaattcttc	attcagaaaa	attatcttag	ggactgatat	60
tggttaattat	ggtcaattta	atwrrtrttk	ggggcatttc	cttacattgt	cttgacaaga	120
ttaaaatgtc	tgtgccaaaa	ttttgtattt	tatttggaga	cttcttatca	aaagtaatgc	180
tgccaaagga	agtctaagga	attagtagtg	ttcccmtcac	ttgtttggag	tgtgctattc	240
taaaagattt	tgatttcctg	gaatgacaat	tatattttta	ctttggtggg	ggaaanagtt	300
ataggaccac	agtcttcact	tctgatactt	gtaaattaat	cttttattgc	acttgttttg	360
accattaagc	tatatgttta	aaa				383

<210> 224

<211> 320

<212> DNA

<213> Homo sapien

<400> 224

ccccgaagg	cttcttggtta	gaaaatagta	cagttacaac	caataggaac	aacaaaaaga	60
aaaagtttgt	gacattgtag	tagggagtgt	gtacccttta	ctcccatca	aaaaaaaaat	120
ggatacatgg	ttaaaggata	raagggaat	attttatcat	atgttctaaa	agagaaggaa	180

gagaaaatac	tactttctcr	aatggaagc	ccttaaaggt	gctttgatac	tgaaggacac	240
aatgtggcc	gtccatcctc	ctttaragtt	gcatgacttg	gacacggtaa	ctgttgacgt	300
tttaractcm	gcattgtgac					320

<210> 225  
 <211> 1214  
 <212> DNA  
 <213> Homo sapien

<400> 225						
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aactcctaca	ccatcggtgt	gggcctgcac	agtcttgagg	ccgaccaaga	gccaggggagc	180
cagatgggtg	aggccagcct	ctccgtacgg	caccagaggt	acaacagacc	cttgctcgct	240
aacgacctca	tgctcatcaa	gttggacgaa	tccgtgtccg	agtctgacac	catccggagc	300
atcagcattg	cttcgcagtg	ccctaccgcg	gggaactctt	gcctcgtttc	tggctggggg	360
ctgctggcga	acggcagaat	gcctaccgtg	ctgcagtgcg	tgaacgtgtc	ggtgggtgtct	420
gaggaggtct	gcagtaagct	ctatgaccgg	ctgtaccacc	ccagcatgtt	ctgcgccggc	480
ggaggggcaag	accagaagga	ctcctgcaac	ggtgactctg	ggggggccct	gatctgcaac	540
gggtacttgc	agggccttgt	gtctttcgga	aaagccccgt	gtggccaagt	tggcgtgcca	600
ggtgtctaca	ccaacctctg	caaatctact	gagtggatag	agaaaaccgt	ccaggccaagt	660
taactctggg	gactgggaac	ccatgaaatt	gacccccaaa	tacatcctgc	ggaaggaatt	720
caggaatatc	tggtcccgag	ccctcctccc	tcaggcccag	gagtcaggc	ccccagcccc	780
tcctccctca	aaccaagggt	acagatcccc	agccccctct	ccctcagacc	caggagtcca	840
gacccccag	cccctcctcc	ctcagaccga	ggagtccagc	ccctcctccc	tcagaccag	900
gagtcagac	ccccagccc	ctcctccctc	agaccaggg	gtccaggccc	ccaaccctc	960
ctccctcaga	ctcagaggtc	caagccccca	acccctcctt	ccccagaccc	agagggtccag	1020
gtccagccc	ctcctccctc	agaccagcg	gtccaatgcc	acctagactc	tcctgtaca	1080
cagtgccccc	ttgtggcacg	ttgacccaac	cttaccagtt	ggtttttcat	ttttgtccc	1140
tttcccctag	atccagaaat	aaagtctaag	agaagcgcaa	aaaaaaaaaa	aaaaaaaaaa	1200
aaaaaaaaaa	aaaa					1214

<210> 226  
 <211> 119  
 <212> DNA  
 <213> Homo sapien

<400> 226						
accagtatg	tgaggggaga	cggaacccca	tgtgacagcc	cactccacca	gggttcccaa	60
agaacctggc	ccagtcataa	tcattcatcc	tgacagtggc	aataatcacg	ataaccagt	119

<210> 227  
 <211> 818  
 <212> DNA  
 <213> Homo sapien

<400> 227						
acaattcata	gggacgacca	atgaggacag	ggaatgaacc	cggtctctcc	ccagccctga	60
tttttgctac	atatgggggc	ccttttcatt	ctttgcaaaa	acactgggtt	ttctgagaac	120
acggacgggt	cttagcacia	tttgtgaaat	ctgtgtaraa	ccgggctttg	caggggagat	180
aattttcctc	ctctggagga	aaggtgggtg	ttgacaggca	gggagacagt	gacaaggcta	240
gagaaagcca	cgctcggcct	tctctgaacc	aggatggaac	ggcagacccc	tgaaaacgaa	300
gcttgctccc	ttccaatcag	ccacttctga	gaacccccat	ctaacttctt	actggaaaag	360
agggcctcct	caggagcagt	ccaagagttt	tcaaagataa	cgtgacaact	accatctaga	420
ggaaaggggtg	caccctcagc	agagaagccg	agagcttaac	tctggctcgtt	tccagagaca	480
acctgctggc	tgtcttgga	tgcgcccagc	ctttgagagg	ccactacccc	atgaacttct	540
gccatccact	ggacatgaag	ctgaggacac	tgggcttcaa	cactgagttg	tcatgagagg	600
gacaggctct	gccctcaagc	cggctgaggg	cagcaaccac	tctcctcccc	tttctcacgc	660
aaagccattc	ccacaaatcc	agaccatacc	atgaagcaac	gagacccaaa	cagtttggtc	720
caagaggata	tgaggactgt	ctcagcctgg	ctttgggctg	acaccatgca	cacacacaag	780
gtccacttct	aggttttcag	cctagatggg	agtcgtgt			818

<210> 228  
 <211> 744  
 <212> DNA  
 <213> Homo sapien

<400> 228  
 actggagaca ctgttgaact tgatcaagac ccagaccacc ccaggtctcc ttcgtgggat 60  
 gtcattgacgt ttgacatacc tttggaacga gcctcctcct tggaagatgg aagaccgtgt 120  
 tcgtggccga cctggcctct cctggcctgt ttcttaagat gcggagtcac atttcaatgg 180  
 taggaaaagt ggcttcgtaa aatagaagag cagtcaactgt ggaactacca aatggcgaga 240  
 tgctcgggtg acattggggg gctttgggat aaaagattta tgagccaact attctctggc 300  
 accagattct aggccagttt gttccactga agcttttccc acagcagtcc acctctgcag 360  
 gctggcagct gaatggcctg ccggtggctc tgtggcaaga tcacactgag atcgatgggt 420  
 gagaaggcta ggatgcttgt ctagtgttct tagctgtcac gttggctcct tccaggttgg 480  
 ccagacggtg ttggccactc ccttctaaaa cacaggcgcc ctctgtgtga cagtgaccgc 540  
 ccgtggtatg ccttggccca ttccagcagt cccagttatg catttcaagt ttgggggttg 600  
 ttcttttctg taatgttctt ctgtgttgtc agctgtcttc atttctctgg ctaagcagca 660  
 ttgggagatg tggaccagag atccactcct taagaaccag tggcgaaaga cactttcttt 720  
 cttcactctg aagtagctgg tgggt 744

<210> 229  
 <211> 300  
 <212> DNA  
 <213> Homo sapien

<400> 229  
 cgagtctggg ttttgtctat aaagtttgat ccctcctttt ctcatccaaa tcatgtgaac 60  
 cattacacat cgaataaaaa gaaagggtggc agacttgccc aacgccaggc tgacatgtgc 120  
 tgcagggttg ttgtttttta attattattg tttagaacgt caccacagt cctgtttaat 180  
 ttgtatgtga cagccaactc tgagaaggtc ctatttttcc acctgcagag gatccagtct 240  
 cactaggctc ctcttgccc tcacactgga gtctccgcca gtgtgggtgc ccactgacat 300

<210> 230  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 230  
 cagcagaaca aatacaata tgaagagtgc aaagatctca taaaatctat gctgaggaat 60  
 gagcgacagt tcaaggagga gaagcttgca gagcagctca agcaagctga ggagctcagg 120  
 caatataaag tctgtgttca cactcaggaa cgagagctga cccagtttaag ggagaagttg 180  
 cgggaaggga gagatgcctc cctctcattg aatgagcatc tccaggccct cctcactccg 240  
 gatgaaccgg acaagtccca ggggcaggac ctccaagaaa cagacctcgg ccgcgacca 300  
 g 301

<210> 231  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 231  
 gcaagcacgc tggcaaactc ctgtcaggtc agctccagag aagccattag tcatttttagc 60  
 caggaactcc aagtcacat ccttggcaac tggggacttg cgagggttag ccttgaggat 120  
 ggcaacacgg gacttctcat caggaagtgg gatgtatg agctgatcaa gacggccagg 180  
 tctgaggatg gcaggatcaa tgatgtcagg ccggttggtg ccgccaatga tgaacacatt 240  
 tttttttgtg gacatgccat ccatttctgt caggatctgg ttgatgactc ggtcagcagc 300  
 c 301

<210> 232  
 <211> 301  
 <212> DNA  
 <213> Homo sapien



<400> 232  
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 ggcgacagcg gggcttcctg attctggaat ataactttgt gtaaattaac agccacctat 120  
 agaagagtcc atctgctgtg aaggagagac agagaactct gggttccgtc gtcctgtcca 180  
 cgtgctgtac caagtgtggt tgcagcctg ttacctgttc tactgaaaa tctggctaata 240  
 gctcttgtgt atcacttctg attctgacaa tcaatcaatc aatggcctag agcactgact 300  
 g 301

<210> 233  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 233  
 atgactgact tccagtaag gctctctaag gggtaagtag gaggatccac aggatttgag 60  
 atgctaaggc cccagagatc gtttgatcca accctcttat tttcagaggg gaaaatgggg 120  
 cctagaagtt acagagcatc tagctgggtc gctggcacc cctggcctcac acagactccc 180  
 gagtagctgg gactacaggc acacagtcac tgaagcaggc cctgttagca attctatgcg 240  
 tacaattaa catgagatga gttagagactt tattgagaaa gcaagagaaa atcctatcaa 300  
 c 301

<210> 234  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 234  
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 cattttattc atcatgatgc tttcttttgt ttcttctttt cgttttcttc ttttctttt 120  
 tcaatttcag caacatactt ctcaatttct tcaggattta aaatcttgag ggattgatct 180  
 cgcctcatga cagcaagtgc aatgtttttg ccacctgact gaaccacttc caggagtggc 240  
 ttgatcacca gcttaatggt cagatcatct gttcaatgg cttcgtcagt atagttcttc 300  
 t 301

<210> 235  
 <211> 283  
 <212> DNA  
 <213> Homo sapien

<400> 235  
 tggggctgtg catcaggcgg gtttgagaaa tattcaattc tcagcagaag ccagaatttg 60  
 aattccctca tcttttaggg aatcatttac caggtttga gaggattcag acagctcagg 120  
 tgctttcact aatgtctctg aacttctgtc cctctttgtt catggatagt ccaataaata 180  
 atgttatctt tgaactgatg ctcataggag agaataaag aactctgagt gatataca 240  
 ttagggatcc aaagaaatat tagatttaag ctcacactgg tca 283

<210> 236  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 236  
 aggtcctcca ccaactgcct gaagcacggt taaaattggg aagaagtata gtgcagcata 60  
 aatactttta aatcgatcag atttccctaa cccacatgca atcttcttca ccagaagagg 120  
 tcggagcagc atcataata ccaagcagaa tgcgtaatag ataaatacaa tggatatag 180  
 tgggtagacg gcttcatgag tacagtgtac tgtggtatcg taatctggac ttgggttgta 240  
 aagcatcgtg taccagtcat aaagcatcaa tactcgacat gaacgaatat aaagaacacc 300  
 a 301

<210> 237  
 <211> 301

<212> DNA  
<213> Homo sapien

<400> 237  
cagtggtagt ggtgggtggac gtggcggttg tctgtggtgcc ttttttgggtg cccgtcacaa 60  
actcaatttt tgttcgctcc tttttggcct ttccaattt gtccatctca attttctggg 120  
ccttggtctaa tgcctcatag taggagtcct cagaccagcc atggggatca aacatatcct 180  
ttgggtagtt ggtgccaagc tctgcaatgg cacagaatgg atcagcttct cgtaaacta 240  
gggttccgaa attctttctt cctttggata atgtagttca tatccattcc ctcctttatc 300  
t 301

<210> 238  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 238  
gggcagggttt tttttttttt ttttttgatg gtgcagaccc ttgctttatt tgtctgactt 60  
gttcacagtt cagccccctg ctcaaaaaac caacgggcca gctaaggaga ggaggaggca 120  
ccttgagact tccggagtcg aggtctctcca gggttcccca gccatcaat cattttctgc 180  
acccctgcc tgggaagcag ctccctgggg ggtgggaatg ggtgactaga agggatttca 240  
gtgtgggacc cagggtctgt tcttcacagt aggaggtgga agggatgact aatttcttta 300  
t 301

<210> 239  
<211> 239  
<212> DNA  
<213> Homo sapien

<400> 239  
ataagcagct aggaattct ttatttagta atgtcctaac ataaaagtgc acataactgc 60  
ttctgtcaaa ccatgatact gagctttgtg acaaccaga aataactaag agaaggcaaa 120  
cataatacct tagagatcaa gaaacattta cacagttcaa ctgtttaaaa atagctcaac 180  
attcagccag tgagtagagt gtgaatgcca gcatacacag tatacaggtc cttcaggga 239

<210> 240  
<211> 300  
<212> DNA  
<213> Homo sapien

<400> 240  
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gggatctgcc ctccagtga accttttaag gaagaagtgg gcccaagcta agttccacat 120  
gctgggtgag ccagatgact tctgttcctt ggtcactttc ttcaatgggg cgaatggggg 180  
ctgccagggt tttaaaatca tgcttcattt tgaagcacac ggtcacttca cctcctcac 240  
gctgtgggtg tactttgatg aaaataccca ctttgttggc ctttctgaag ctataatgtc 300

<210> 241  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 241  
gaggtctggt gctgaggtct ctgggctagg aagaggagtt ctgtggagct ggaagccaga 60  
cctcttttga ggaaactcca gcagctatgt tgggtgtctt gagggaatgc aacaaggctg 120  
ctcctccatg tattggaaaa ctgcaaaactg gactcaactg gaaggaagtg ctgctgccag 180  
tgtgaagaac cagcctgagg tgacagaaaac ggaagcaaac aggaacagcc agtcttttct 240  
tcctcctcct gtcatacggg ctctctcaag catcctttgt tgtcaggggc ctaaaaggga 300  
g 301

<210> 242  
<211> 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 242

ccgagggtcct	gggatgcaac	caatcactct	gtttcacgtg	acttttatca	ccatacaatt	60
tgtggcattt	cctcattttc	tacattgtag	aatcaagagt	gtaaataaat	gtatatcgat	120
gtcttcaaga	atatatcatt	cctttttcac	tagaaccat	tcaaaatata	agtcaagaat	180
cttaatatca	acaaatatat	caagcaaact	ggaaggcaga	ataactacca	taatttagta	240
taagtaccga	aagttttata	aatcaaaagc	cctaattgata	accattttta	gaattcaatc	300
a						301

&lt;210&gt; 243

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 243

aggtaagtcc	cagtttgaag	ctcaaaagat	ctgggtatgag	cataggctca	tcgacgacat	60
ggtggcccaa	gctatgaaat	cagagggagg	cttcatctgg	gcctgtaaaa	actatgatgg	120
tgacgtgcag	tcggactctg	tgccccagg	gtatggctct	ctcggcatga	tgaccagcgt	180
gctggtttgt	ccagatggca	agacagtaga	agcagaggct	gcccacggga	ctgtaacccg	240
tcaactaccg	atgttcaga	aaggacagga	gacgtccacc	aatcccattg	cttccatfff	300
t						301

&lt;210&gt; 244

&lt;211&gt; 300

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 244

gctggtttgc	aagaatgaaa	tgaatgattc	tacagctagg	acttaacctt	gaaatggaaa	60
gtcatgcaat	ccattttgca	ggatctgtct	gtgcacatgc	ctctgtagag	agcagcattc	120
ccagggacct	tggaacagat	tgacactgta	agggtgcttg	tccccaaagac	acatcctaaa	180
agggtgttga	atggtgaaaa	cgtcttcctt	ctttattggc	ccttcttatt	tatgtgaaca	240
actgtttgtc	ttttgtgtat	cttttttaaa	ctgtaaagtt	caattgtgaa	aatgaatatc	300

&lt;210&gt; 245

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 245

gtctgagtat	ttaaaatggt	attgaaatta	tccccaacca	atgttagaaa	agaaagaggt	60
tatatactta	gataaaaaat	gaggtgaatt	actatccatt	gaaatcatgc	tcttagaatt	120
aaggccagga	gatattgtca	ttaatgtara	cttcaggaca	ctagagtata	gcagccctat	180
gttttcaaag	agcagagatg	caattaaata	ttgttttagca	tcaaaaaggc	cactcaatac	240
agctaataaa	atgaaagacc	taattttctaa	agcaattctt	tataatttac	aaagtfttaa	300
g						301

&lt;210&gt; 246

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 246

ggtctgtcct	acaatgcctg	cttcttgaaa	gaagtcggca	ctttctagaa	tagctaaata	60
acctgggctt	atfttaaaaga	actatttgta	gtcagatttg	gttttcctat	ggctaaaata	120
atgcttctt	gtgaaaatta	aataaaacag	ttaattcaaa	gccttgatat	atgttaccac	180
taacaatcat	actaaatata	ttttgaagta	caaagtttga	catgctctaa	agtgacaacc	240
caaagtgtgc	ttacaaaaca	cgttcctaac	aaggtatgct	ttacactacc	aatgcagaaa	300
c						301

<210> 247  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 247  
 aggtcctttg gcagggctca tggatcagag ctcaaactgg agggaaaggc atttcgggta 60  
 gcctaagagg gcgactggcg gcagcacaac caaggaaggc aagggtgttt cccccacgct 120  
 gtgtcctgtg ttcaggtgcg acacacaatc ctcatgggaa caggatcacc catgcgctgc 180  
 ccttgatgat caaggttggg gcttaagtgg attaagggag gcaagttctg gggttccttg 240  
 cttttcaaac catgaagtca ggctctgtat ccctcctttt cctaactgat attctaacta 300  
 a 301

<210> 248  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 248  
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 attaggaaga ttcttagggg taatttttct gaggaaggag aactagccaa cttaagaatt 120  
 acaggaagaa agtgggttgg aagacagcca aagaaataaa agcagattaa attgtatcag 180  
 gtacattcca gcctgttggc aactccataa aaacatttca gattttaatc ccgaatttag 240  
 ctaatgagac tggatttttg ttttttatgt tgtgtgtcgc agagctaaaa actcagttcc 300  
 c 301

<210> 249  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 249  
 gtccagagga agcacctggt gctgaactag gcttgccctg ctgtgaactt gcacttggag 60  
 ccctgacgct gctgttctcc ccgaaaaaacc cgaccgacct ccgcgatctc cgtcccgcc 120  
 ccagggagac acagcagtga ctccagagctg gtgcgacact gtgcctccct cctcaccgcc 180  
 catcgtaatg aattattttg aaaattaatt ccaccatcct ttcagattct ggatggaaag 240  
 actgaatctt tgactcagaa ttgtttgctg aaaagaatga tgtgactttc ttagtcattt 300  
 a 301

<210> 250  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 250  
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 cttatcttta ttggcttgat aaacataatt atttctaaca ctactttatt tccagttgcc 120  
 cataagcaca tcagtacttt tctctggctg gaatagtaaa cttaaagtatg gtacatctac 180  
 ctaaaagact actatgtgga ataatacata ctaatgaagt attacatgat ttaaagacta 240  
 caataaaacc aaacatgctt ataacattaa gaaaaacaat aaagatacat gattgaaacc 300  
 a 301

<210> 251  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 251  
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 gccaggggtc ctcaaaaatg ccactgtcac tgccaggaaa tgcttctgag cagtacacct 180  
 cattgggatc aatgaaaagc ttcaagaaat cttcaggctc actctcttga aggcccgga 240

cctctggagg ggggcagtgg aatcccagct ccaggacgga tcctgtcgaa aagatatacct 300  
c 301

<210> 252  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 252  
gcaaccaatc actctgtttc acgtgacttt tatcaccata caatttggtg catttcctca 60  
ttttctacat tgtagaatca agagtgtaaa taaatgtata tcgatgtctt caagaatata 120  
tcatttccttt ttcactagga acccattcaa aatataagtc aagaatctta atatcaacaa 180  
atatatcaag caaactggaa ggcagaataa ctaccataat ttagtataag tacccaaagt 240  
tttataatc aaaagcccta atgataacca tttttagaat tcaatcatca ctgtagaatc 300  
a 301

<210> 253  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 253  
ttccctaaga agatgttatt ttgttgggtt ttgttccccc tccatctcga ttctcgtacc 60  
caactaaaaa aaaaaaataa agaaaaaatg tgctgcgttc tgaaaaataa ctccttagct 120  
tggtctgatt gttttcagac cttaaaatat aaacttggtt cacaagcttt aatccatgtg 180  
gatttttttt cttagagaac cacaaaacat aaaaggagca agtcggactg aatacctgtt 240  
tccatagtgc ccacagggtg ttctcacat tttctccata ggaaaatgct ttttccaag 300  
g 301

<210> 254  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 254  
cgctgcgcct ttcccttggg ggaggggcaa ggccagaggg ggtccaagtg cagcacgagg 60  
aacttgacca attcccttga agcgggtggg ttaaaccctg taaatgggaa caaaatcccc 120  
ccaaatctct tcatcttacc ctggtggact cctgactgta gaattttttg gttgaacaa 180  
gaaaaaataa aagcttttga cttttcaagg ttgcttaaca ggtactgaaa gactggcctc 240  
acttaaactg agccaggaaa agctgcagat ttattaatgg gtgtgttagt gtgcagtgcc 300  
t 301

<210> 255  
<211> 302  
<212> DNA  
<213> Homo sapien

<400> 255  
agcttttttt tttttttttt tttttttttt ttcattaaaa aatagtgtct tttattataa 60  
attactgaaa tgtttctttt ctgaatataa atataaatat gtgcaaagtt tgacttggat 120  
tgggattttg ttgagtctt caagcatctc ctaataccct caaggcctg agtagggggg 180  
aggaaaaagg actggagggt gaatctttat aaaaaacaag agtgattgag gcagattgta 240  
aacattatta aaaaacaaga aacaaacaaa aaaatagaga aaaaaaccac cccaacacac 300  
aa 302

<210> 256  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 256

```

gttccagaaa acattgaagg tggtttccca aagtctaact agggatacc cctctagcct    60
aggacctcc  tccccacacc tcaatccacc aaaccatcca taatgcaccc agataggccc    120
acccccaaaa gcctggacac cttgagcaca cagttatgac caggacagac tcatctctat    180
aggcaaatag ctgctggcaa actggcatta cctggtttgt ggggatggg gggcaagtgt    240
gtggcctctc ggcttggtta gcaagaacat tcagggtagg cctaagttaa tcgtgttagt    300
t                                                    301

```

&lt;210&gt; 257

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 257

```

gttgtggagg aactctggct tgctcattaa gtctactga ttttcactat cccctgaatt    60
tccccactta tttttgtctt tcactatcgc aggccttaga agaggtctac ctgcctccag    120
tcttaacctag tccagtctac cccctggagt tagaatggcc atcctgaagt gaaaagtaat    180
gtcacattac tccttccagt gatttcttgt agaagtgcc atccctgaat gccaccaaga    240
tcttaattctt cacatcttta atcttatctc ttgactcct ctttacaccg gagaaggctc    300
c                                                    301

```

&lt;210&gt; 258

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 258

```

cagcagtagt agatgccgta tgccagcacg cccagcactc ccaggatcag caccagcacc    60
agggggcccag ccaccaggcg cagaagcaag ataaacagta ggctcaagac cagagccacc    120
cccaggggcaa caagaatcca ataccaggac tggggcaaat cttcaaatgat cttaacactg    180
atgtctcggg cattgaggct gtcaataana cgctgatccc ctgctgtatg gtggtgtcat    240
tggtgatccc tgggagcgcc ggtggagtaa cgttggtcca tggaaagcag cgcccacaac    300
t                                                    301

```

&lt;210&gt; 259

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 259

```

tcatatatgc aaacaaatgc agactangcc tcaggcagag actaaaggac atctcttggg    60
gtgtcttgaa gtgatttgga cccctgaggg cagacaccta agtaggaatc ccagtgggaa    120
gcaaagccat aaggaagccc aggattcctt gtgatcagga agtgggccag gaaggtctgt    180
tccagctcac atctcatctg catgcagcac ggaccggatg cgcccactgg gtcttggtt    240
ccctcccatc ttctcaagca gtgtccttgt tgagccattt gcatccttgg ctccaggtgg    300
c                                                    301

```

&lt;210&gt; 260

&lt;211&gt; 301

<212> DNA  
<213> Homo sapien

<400> 260  
 ttttttttct ccctaaggaa aaagaaggaa caagtctcat aaaaccaa at aagcaatggt 60  
 aagggtgtctt aacttgaaaa agattaggag tcaactggttt acaagttata attgaatgaa 120  
 agaactgtaa cagccacagt tggccatttc atgccaatgg cagcaacaa caggattaac 180  
 tagggcaaaa taaataagtg tgtggaagcc ctgataagtg cttataaac agactgattc 240  
 actgagacat cagtacctgc ccgggcggcc gctcgagccg aattctgcag atatccatca 300  
 c 301

<210> 261  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 261  
 aaatattcga gcaaactctg taactaatgt gtctccataa aaggctttga actcagtga 60  
 tctgcttcca tccacgattc tagcaatgac ctctcggaca tcaaagctcc tcttaagggt 120  
 agcaccaact attccataca attcatcagc aggaaataaa ggctcttcag aagggtcaat 180  
 ggtgacatcc aatttcttct gataatttag attcctcaca accttcctag ttaagtgaag 240  
 ggcattgatga tcatccaaag cccagtggtc acttactcca gactttctgc aatgaagatc 300  
 a 301

<210> 262  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 262  
 gaggagagcc tgttacagca tttgtaagca cagaatactc caggagtatt tgtaattgtc 60  
 tgtgagcttc ttgccgcaag tctctcagaa atttaaaaag atgcaaatcc ctgagtcacc 120  
 cctagacttc ctaaacagca tcctctgggg ctggaacctg gcactctgca tttgtaatga 180  
 gggctttctg gtgcacacct aattttgtgc atctttgccc taaatcctgg attagtgtcc 240  
 catcattacc cccacattat aatgggatag attcagagca gatactctcc agcaaagaat 300  
 c 301

<210> 263  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

<400> 263  
 tttagcttgt ggtaaatgac tcacaaaact gattttaaaa tcaagttaat gtgaattttg 60  
 aaaattacta cttaatccta attcacaata acaatggcat taaggtttga ctgagttgg 120  
 ttcttagtat tatttatggt aaataggctc ttaccacttg caaataactg gccacatcat 180  
 taatgactga cttcccagta aggtctctta aggggtaagt angaggatcc acaggatttg 240  
 agatgctaag gccccagaga tcgtttgatc caaccctctt attttcagag gggaaaatgg 300  
 g 301

<210> 264  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 264  
 aaagacgtta aaccactcta ctaccacttg tggaaactctc aaagggttaa tgacaaascc 60

aatgaatgac	tctaaaaaca	atattttacat	ttaatggttt	gtagacaata	aaaaaacaag	120
gtggatagat	ctagaattgt	aacattttta	gaaaaccata	scatttgaca	gatgagaaag	180
ctcaattata	gatgcaaagt	tataactaaa	ctactatagt	agtaaagaaa	tacatttcac	240
acccttcata	taaattcact	atcttggtt	gaggcactcc	ataaaatgta	tcacgtgcat	300
a						301

<210> 265  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 265	
tgcccaagtt	atgtgtaagt
gtatccgcac	ccagaggtaa
aactacactg	tcattcttgt
60	
cttcttgtga	cgagtatatt
cttctctggg	gagaagccgg
gaagtcttct	cctggctcta
120	
catattcttg	gaagtctcta
atcaactttt	gttccatttg
tttcatttct	tcaggaggga
180	
ttttcagttt	gtcaacatgt
tctctaacaa	cacttgccca
tttctgtaaa	gaatccaaag
240	
cagtccaagg	ctttgacatg
tcaacaacca	gcataactag
agtatccttc	agagatacgg
300	
c	
	301

<210> 266  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 266	
taccgtctgc	ccttcctccc
atccaggcca	tctgccaatc
tacatgggtc	ctcctattcg
60	
acaccagatc	actctttcct
ctacccacag	gcttgctatg
agcaagagac	acaacctcct
120	
ctctctgtg	ttccagcttc
ttttcctgtt	cttcccaccc
cttaagtctt	attcctgggg
180	
atagagacac	caatacccat
aacctctctc	ctaagcctcc
ttataacca	gggtgcacag
240	
cacagactcc	tgacaactgg
taaggccaat	gaactgggag
ctcacagctg	gctgtgcctg
300	
a	
	301

<210> 267  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 267	
aaagagcaca	ggccagctca
gcctgccctg	gccatctaga
ctcagcctgg	ctccatgggg
60	
gttctcagtg	ctgagtcctt
ccaggaaaag	ctcacctaga
ccttctgagg	ctgaatcttc
120	
atcctcacag	gcagcttctg
agagcctgat	attcctagcc
ttgatggctt	ggagttaagc
180	
ctcattctga	ttcctctcct
tcttttcttt	caagttggct
ttcctcacat	ccctctgttc
240	
aattcgcttc	agcttgctctg
ctttagccct	catttcaga
agcttcttct	ctttggcatc
300	
t	
	301

<210> 268  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 268	
aatgtctcac	tcaactactt
cccagcctac	cgtggcctaa
ttctgggagt	tttcttctta
60	
gatcttggga	gagctgggtc
ttctaaggag	aaggaggaaag
gacagatgta	actttggatc
120	
tcgaagagga	agtctaattg
aagtaattag	tcaacggctc
ttgttttagac	tcttgggaata
180	
tgctgggttg	ctcagtgagc
ccttttggag	aaagcaagta
ttattcttaa	ggagtacca
240	
cttcccattg	ttctactttc
taccatcatc	aattgtatat
tatgtattct	ttggagaact
300	
a	
	301

<210> 269  
 <211> 301  
 <212> DNA  
 <213> Homo sapien



<400> 269  
 taacaatata cactagctat ctttttaact gtccatcatt agcaccaatg aagattcaat 60  
 aaaattacct ttattcacac atctcaaaac aattctgcaa attcttagtg aagtttaact 120  
 atagtcacag accttaata ttcacattgt tttctatgtc tactgaaaat aagttcacta 180  
 cttttctgga tattctttac aaaatcttat taaaattcct ggtattatca cccccaatta 240  
 tacagtagca caaccacctt atgtagtttt tacatgatag ctctgtagaa gtttcacatc 300  
 t 301

<210> 270  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 270  
 cattgaagag cttttgcgaa acatcagaac acaagtgcct ataaaattaa ttaagcctta 60  
 cacaagaata catattcctt ttatttctaa ggagttaaac atagatgtag ctgatgtgga 120  
 gagcttgctg gtgcagtgca tattggataa cactattcat ggccgaattg atcaagtcaa 180  
 ccaactcctt gaactggatc atcagaagaa ggggtggtgca cgatatactg cactagataa 240  
 tggaccaacc aactaaattc tctcaccagg ctgtatcagt aaactggctt aacagaaaac 300  
 a 301

<210> 271  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 271  
 aaaaggttct cataagatta acaatttaaa taaatatttg atagaacatt ctttctcatt 60  
 tttatagctc atctttaggg ttgatattca gttcatgcct cccttgctgt tcttgatcca 120  
 gaattgcaat cacttcatca gcctgtattc gctccaattc tctataaagt ggggtccaagg 180  
 tgaaccacag agccacagca cacctctttc ccttggtgac tgccttcacc ccatganggt 240  
 tctctcctcc agatganaac tgatcatgcg cccacatttt ggggttttata gaagcagtc 300  
 c 301

<210> 272  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 272  
 taaattgcta agccacagat aacaccaatc aaatggaaca aatcactgtc ttcaaattgc 60  
 ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtatttagga 120  
 tccaataatt ccctcatgat gagcaagaaa aattctttgc gcacccctcc tgcatecaca 180  
 gcatcttctc caacaaatat aaccttgagt ggcttcttgt aatctatgtt ctttgttttc 240  
 ctaaggactt ccattgcac tccataata ttttctctac gcaccactag aattaagcag 300  
 g 301

<210> 273  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

&lt;400&gt; 273

```

acatgtgtgt atgtgtatct ttgggaaaaan aanaagacat cttgtttayt attttttttg      60
agagangctg ggacatggat aatcacwtaa tttgctayta tyactttaat ctgactygaa      120
gaaccgtcta aaaaataaaat ttaccatgtc dtatatccct tatagtatgc ttatttcacc      180
ttytttctgt ccagagagag tatcagtgac ananatttma ggggtgaamac atgmattggt      240
gggacttnty tttaengam accctgcccg sgcgccctcg makengantt ccgcsananc      300
t                                                                    301

```

&lt;210&gt; 274

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 274

```

cttatatact ctttctcaga ggcaaaagag gagatgggta atgtagacaa ttctttgagg      60
aacagtaaat gattattaga gagaangaat ggaccaagga gacagaaatt aacttgtaaa      120
tgattctctt tggaatctga atgagatcaa gaggccagct ttagcttggt gaaaagtcca      180
tctagggtatg gttgcattct cgtcttcttt tctgcagtag ataatgaggt aaccgaaggc      240
aattgtgctt cttttgataa gaagctttct tggatcatatc aggaaattcc aganaaaagtc      300
c                                                                    301

```

&lt;210&gt; 275

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1)...(301)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 275

```

tcggtgtcag cagcacgtgg cattgaacat tgcaatgtgg agcccaaacc acagaaaatg      60
gggtgaaatt ggccaacttt ctattaactt atgttggtgaa ttttgccacc aacagtaagc      120
tggcccttct aataaaagaa aattgaaagg tttctcacta aacggaatta agtagtgagg      180
taaagagact cccaggcctc agcgtacctg cccggggcggc cgctcgaagc cgaattctgc      240
agatatccat cacactggcg gncgctcgan catgcatcta gaaggnccaa ttcgccctat      300
a                                                                    301

```

&lt;210&gt; 276

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 276

```

tgtacacata ctcaataaat aaatgactgc attgtggtat tattactata ctgattatat      60
ttatcatgtg acttctaatt agaaaatgta tccaaaagca aaacagcaga tatacaaaat      120
taaagagaca gaagatagac attaacagat aaggcaactt atacattgag aatccaaatc      180
caatacattt aaacatttgg gaaatgaggg ggacaaatgg aagccagatc aaatttgtgt      240
aaaactattc agtatgtttc ccttgcttca tgtctgagaa ggctctcctt caatggggat      300
g                                                                    301

```

&lt;210&gt; 277

&lt;211&gt; 301

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 277  
 tttgttgatg tcagtatattt attactttgcg ttatgagtgc tcacctggga aattctaaag 60  
 atacagagga cttggaggaa gcagagcaac tgaatttaat ttaaaagaag gaaaacattg 120  
 gaatcatggc actcctgata ctttcccaaa tcaacactct caatgccccca ccctcgctct 180  
 caccatagtg gggagactaa agtggccacg gatttgcctt angtgtgcag tgcgttctga 240  
 gttcncctgtc gattacatct gaccagtctc ctttttccga agtcnctccg ttcaatcttg 300  
 c 301

<210> 278  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 278  
 taccactaca ctccagcctg ggcaacagag caagacctgt ctcaaagcat aaaatggaat 60  
 aacatatcaa atgaaacagg gaaaatgaag ctgacaattt atggaagcca gggcttgtca 120  
 cagctctctac tgttattatg cattacctgg gaatttatat aagcccttaa taataatgcc 180  
 aatgaacatc tcattgtgtgc tcacaatgtt ctggcactat tataagtgtc tcacaggttt 240  
 tatgtgttct tcgtaacttt atggantagg tactcggccg cgaacacgct aagccgaatt 300  
 c 301

<210> 279  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 279  
 aaagcaggaa tgacaaagct tgcttttctg gtatgttcta ggtgtattgt gacttttact 60  
 gttatattaa ttgccaatat aagtaaatat agattatata tgtatagtgt ttcacaaagc 120  
 ttagaccttt accttccagc caccacacag tgcttgatat ttcagagtca gtcattgggt 180  
 atacatgtgt agttccaaag cacataagct agaanaanaa atatttctag ggagcactac 240  
 catctgtttt cacatgaaat gccacacaca tagaactcca acatcaattt cattgcacag 300  
 a 301

<210> 280  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 280  
 ggtactggag ttttctctcc ctgtgaaaac gtaactactg ttgggagtga attgaggatg 60  
 tagaaagggt gtggaaccaa attgtgggtca atggaaatag gagaatatgg ttctcactct 120  
 tgagaaaaaa acctaaagatt agcccaggta gttgcctgta acttcagttt ttctgcctgg 180  
 gtttgatata gtttaggggt gggttagat taagatctaa attacatcag gacaaagaga 240  
 cagactatta actccacagt taattaagga ggtatgttcc atgtttattt gttaaagcag 300  
 t 301

86

<210> 281  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 281  
 aggtacaaga aggggaatgg gaaagagctg ctgctgtggc attgttcaac ttggatattc 60  
 gccgagcaat ccaaattcctg aatgaagggg catcttctga aaaaggagat ctgaatctca 120  
 atgtggtagc aatggcttta tcgggttata cggatgagaa gaactccctt tggagagaaa 180  
 tgtgtagcac actgcgatta cagctaaata acccgtattt gtgtgtcatg tttgcatttc 240  
 tgacaagtga aacaggatct tacgatggag ttttgtatga aaacaaagtt gcagtacctc 300  
 g 301

<210> 282  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 282  
 caggtactac agaattaaaa tactgacaag caagtagttt cttggcgtgc acgaattgca 60  
 tccagaacct aaaaatttaag aaattcaaaa agacattttg tgggcacctg ctgacacaga 120  
 agcgcagaag caaagcccag gcagaacctat gctaaccctta cagctcagcc tgcacagaag 180  
 cgcagaagca aagcccaggc agaaccatgc taaccttaca gctcagcctg cacagaagcg 240  
 cagaagcaaa gccccaggcag aacatgctaa ccttacagct cagcctgcac agaagcacag 300  
 a 301

<210> 283  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 283  
 atctgtatac ggcagacaaa ctttatarag tgtagagagg tgagcgaaag gatgcaaaag 60  
 cactttgagg gctttataat aatatgctgc ttgaaaaaaa aaatgtgtag ttgatactca 120  
 gtgcatctcc agacatagta aggggttgct ctgaccaatc aggtgatcat tttttctatc 180  
 acttcccagg ttttatgcaa aaattttgtt aaattctata atggtgatat gcattcttta 240  
 ggaaacatat acatttttaa aaatctattt tatgtaagaa ctgacagacg aatttgcttt 300  
 g 301

<210> 284  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 284  
 caggtacaaa acgctattaa gtggcttaga atttgaacat ttgtggtctt tatttacttt 60  
 gcttcgtgtg tgggcaaagc aacatcttcc ctaaatatat attaccaaga aaagcaagaa 120  
 gcagattagg tttttgacaa aacaaaacagg ccaaaaagggg gctgacctgg agcagagcat 180  
 ggtgagaggc aaggcatgag agggcaagtt tgttgtggac agatctgtgc ctactttatt 240  
 actggagtaa aagaaaacaa agttcattga tgtcgaagga tatatacagt gttagaaatt 300  
 a 301

<210> 285  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 285  
 acatcacat gatcggatcc cccacccatt atacgttgta tgtttacata aatactcttc 60  
 aatgatcatt agtggtttta aaaaaatact gaaaactcct tctgcatccc aatctctaac 120  
 caggaaagca aatgctatct acagacctgc aagccctccc tcaaacnaaa ctatttctgg 180  
 attaaatag tctgacttct tttgaggtca cagcactagg caaatgctat ttacgatctg 240  
 caaagctgt ttgaagagtc aaagcccca tgtgaacacg atttctggac cctgtaacag 300  
 t 301

<210> 286  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 286  
 taccactgca ttccagcctg ggtgacagag tgagactccg tctccaaaaa aaactttgct 60  
 tgtatattat ttttgctta cagtggatca ttctagtagg aaaggacagt aagatttttt 120  
 atcaaatgt gtcatgccag taagagatgt tatattcttt tctcatttct tccccacca 180  
 aaaataagct accatatagc ttataagtct caaatttttg ccttttacta aaatgtgatt 240  
 gtttctgttc attgtgatg cttcatcacc tatattaggc aaattccatt ttttcccttg 300  
 t 301

<210> 287  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 287  
 tacagatctg ggaactaaat attaaaaatg agtgtggctg gatatatgga gaatgttggg 60  
 ccagaaagga acgtagagat cagatattac aacagctttg ttttgagggt tagaaatatg 120  
 aaatgatttg gttatgaacg cacagttag gcagcagggc cagaatcctg accctctgcc 180  
 ccgtggttat ctctcccca gcttggctgc ctcatgttat cacagtattc cattttgttt 240  
 gttgcatgtc ttgtgaagcc atcaagattt tctcgtctgt tttcctctca ttggtaatgc 300  
 t 301

<210> 288  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 288  
 gtacacctaa ctgcaaggac agctgaggaa tgtaatgggc agccgctttt aaagaagtag 60  
 agtcaatagg aagacaaatt ccagttccag ctcatctgga gtatctgcaa agctgcaaaa 120  
 gatcttttaa gacaatttca agagaatatt tccttaaagt tggcaatttg gagatcatac 180  
 aaaagcatct gcttttgtga tttaatttag ctcatctggc cactggaaga atccaaacag 240  
 tctgccttaa ttttgatga atgcatgatg gaaattcaat aatttagaaa gttaaaaaaa 300  
 a 301

<210> 289  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 289  
 ggtacactgt ttccatgtta tgtttotaca cattgctacc tcagtgtctc tggaaactta 60  
 gcttttgatg tctccaagta gtccaccttc atttaactct ttgaaactgt atcatctttg 120  
 ccaagtaaga gtggtggcct atttcagctg ctttgacaaa atgactggct cctgacttaa 180

```

cggtctataa atgaatgtgc tgaagcaaag tgcccatggt ggcggcgaan aagagaaaaga 240
tgtgttttgt ttggactct ctgtggtccc ttccaatgct gtgggtttcc aaccagnnga 300
a 301

```

```

<210> 290
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 290
acaçtgagct cttcttgata aatatacaga atgcttggca tatacaagat tctatactac 60
tgactgatct gttcatttct ctcacagctc ttacccccaa aagcttttcc accctaagtg 120
ttctgacctc cttttctaata cacagtaggg atagaggcag anccacctac aatgaacatg 180
gagttctatc aagaggcaga aacagcacag aatcccagtt ttaccattcg ctagcagtgc 240
tgçcttgaac aaaaacattt ctccatgtct cattttcttc atgcctcaag taacagtgag 300
a 301

```

```

<210> 291
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 291
caggtaccaaa tttcttctat cctagaaaca tttcatttta tgttgttgaa acataacaac 60
tatatcagct agattttttt tctatgcttt acctgctatg gaaaatttga cacattctgc 120
tttactcttt tgtttatagg tgaatcacaa aatgtatttt tatgtattct gtagttcaat 180
agccatggct gtttacttca ttttaatttat ttagcataaa gacattatga aaaggcctaa 240
acatgagctt cacttcccca ctaactaatt agcatctggt atttcttaac cgtaatgcct 300
a 301

```

```

<210> 292
<211> 301
<212> DNA
<213> Homo sapien

```

```

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

```

```

<400> 292
acçtttttagt agtaatgtct aataataaat aagaaatcaa ttttataagg tccatatagc 60
tgtattaaat aattttttaag tttaaaagat aaaataccat cattttaaat gttggtattc 120
aaaaccaaag natataaccg aaaggaaaaa cagatgagac ataaaatgat ttgcnagatg 180
ggaaatatag tasttyatga atgttnatta aattccagtt ataatagtgg ctacacactc 240
tçactacaca cacagacccc acagtcctat atgccacaaa cacatttcca taacttgaaa 300
a 301

```

```

<210> 293
<211> 301
<212> DNA
<213> Homo sapien

```

```

<400> 293
ggtaccaagt gctgggtgcca gcctgttacc tgttctcact gaaaagtctg gctaatgctc 60
ttgtgtagtc acttctgatt ctgacaatca atcaatcaat ggcctagagc actgactgtt 120
aacacaaacg tçactagcaa agtagcaaca gçtttaagtc taaatacaaa gctgttctgt 180

```

gtgagaattt tttaaaaggc tacttgtata ataacccttg tcatttttaa tgtacctcgg 240  
 ccgcgaccac gctaagccga attctgcaga tatccatcac actggcggcc gctcgagcat 300  
 g 301

<210> 294  
 <211> 301  
 <212> DNA  
 <213> Homo sapien  
 <220>  
 <221> misc\_feature  
 <222> (1)...(301)  
 <223> n = A,T,C or G

<400> 294  
 tgacccataa caatatacac tagctatctt tttaaactgtc catcattagc accaatgaag 60  
 attcaataaa attaccttta ttcacacatc tcaaaacaat tctgcaaatt cttagtgaag 120  
 tttaaactata gtcacaganc ttaaattatc acattgtttt ctatgtctac tgaaaataag 180  
 ttcactactt ttctgggata ttctttacaa aatcttatta aaattcctgg tattatcacc 240  
 ccaattata cagtagcaca accaccttat gtagttttta catgatatgct ctgtagaggt 300  
 t 301

<210> 295  
 <211> 305  
 <212> DNA  
 <213> Homo sapien

<400> 295  
 gtactctttc tctcccctcc tctgaattta attctttcaa cttgcaattt gcaaggatta 60  
 cacattttcac tgtgatgtat attgtgttgc aaaaaaaaaa gtgtctttgt ttaaaattac 120  
 ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccattctctga 180  
 actggtagaa aaacrtctga agagctagtc tatcagcatc tgacagggtga attggatggt 240  
 tctcagaacc atttcaccca gacagcctgt ttctatcctg ttttaataaat tagtttgggt 300  
 tctct 305

<210> 296  
 <211> 301  
 <212> DNA  
 <213> Homo sapien

<400> 296  
 aggtactatg ggaagctgct aaaataatat ttgatagtaa aagtatgtaa tgtgctatct 60  
 cacctagtag taaactaaaa ataaactgaa actttatgga atctgaagtt attttccttg 120  
 attaaataga attaataaac caatatgagg aaacatgaaa ccattgcaatc tactatcaac 180  
 tttgaaaaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataagtcatt 240  
 tgtcattact ataaatttta aaatctgtta ataagatggc ctatagggag gaaaaagggg 300  
 c 301

<210> 297  
 <211> 300  
 <212> DNA  
 <213> Homo sapien

<220>  
 <221> misc\_feature  
 <222> (1)...(300)  
 <223> n = A,T,C or G

<400> 297  
 actgagtttt aactggacgc caagcaggca aggctggaag gttttgctct ctttgtgcta 60  
 aaggttttga aaaccttgaa ggagaatcat ttgacaaga agtacttaag agtctagaga 120  
 acaaagangt gaaccagctg aaagctctcg ggggaanctt acatgtgttg ttaggcctgt 180

tccatcattg ggagtgcact ggccatccct caaaatttgt ctgggctggc ctgagtggtc 240  
accgcacctc ggccgcgacc acgctaagcc gaattctgca gatatccatc acactggcgg 300

<210> 298  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

<400> 298  
tatggggttt gtcacccaaa agctgatgct gagaaaggcc tccctggggc ccctcccgcg 60  
ggcatctgag agacctggtg ttccagtgtt tctggaaatg ggtcccagtg ccgccggctg 120  
tgaagctctc agatcaatca cgggaagggc ctggcggtgg tggccacctg gaaccaccct 180  
gtcctgtctg tttacatttc actaycaggt tttctctggg cattacnatt tgttccccta 240  
caacagtgc ctgtgcattc tgctgtggcc tgctgtgtct gcaggtggct ctcagcgagg 300  
t 301

<210> 299  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 299  
gttttgagac ggagtttcac tcttgttgcc cagactggac tgcaatggca gggctctctgc 60  
tcaactgcacc ctctgcctcc caggttcgag caattctcct gcctcagcct ccaggtagc 120  
tgggattgca ggctcacgcc accataccca gctaattttt ttgtattttt agtagagacg 180  
gagtttcgcc atgttggcca gctgggtctca aactcctgac ctcaagcgac ctgcctgcct 240  
cggcctccca aagtgcgtga attataggca tgagtcaaca cgccagcct aaagatattt 300  
t 301

<210> 300  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 300  
attcagtttt atttgcctgc ccagtatctg taaccaggag tgccacaaaa tcttgccaga 60  
tatgtcccac acccactggg aaaggctccc acctggctac ttcctctatc agctgggtca 120  
gtcgcattcc acaaggttct cagcctaatt agtttacta cctgccagtc tcaaaactta 180  
gtaaagcaag accatgacat tccccacgg aaatcagagt ttgccccacc gtcttgttac 240  
tataaagcct gcctctaaca gtccttgctt cttcacacca atcccagcgc catcccccat 300  
g 301

<210> 301  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 301  
ttaaattttt gagaggataa aaaggacaaa taatctagaa atgtgtcttc ttcagtctgc 60  
agaggacccc aggtctccaa gcaaccacat ggtcaagggc atgaataatt aaaagttggg 120  
gggaactcac aaagaccctc agagctgaga ccccacaac agtgggagct cacaaagacc 180  
ctcagagctg agacaccac aacagtggga gctcacaag accctcagag ctgagacacc 240  
cacaacagca cctcgttcag ctgccacatg tgtgaataag gatgcaatgt ccagaagtgc 300  
t 301

<210> 302  
<211> 301



<212> DNA  
<213> Homo sapien

<400> 302  
aggtacacat ttagcttgtg gtaaagtgact cacaaaactg attttaaaat caagttaatg 60  
tgaattttga aaattactac ttaatcctaa ttcacaataa caatggcatt aagggtttgac 120  
ttgagttggg tcttagtatt atttatggta aatagggtct taccacttgc aaataactgg 180  
ccacatcatt aatgactgac ttcccagtaa ggctctctaa ggggtaagta ggaggatcca 240  
caggatttga gatgctaagg ccccagagat cgtttgatcc aaccctcta ttttcagagg 300  
g 301

<210> 303  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 303  
aggtaccaac tgtggaaata ggtagaggat cattttttct ttccatatca actaagttgt 60  
atattgtttt ttgacagttt aacacatctt cttctgtcag agattctttc acaatagcac 120  
tggctaattg aactaccgct tgcattgtaa aaatgggtgt ttgtgaaatg atcataggcc 180  
agtaacgggt atgtttttct aactgatctt ttgctcgttc caaagggacc tcaagacttc 240  
catcgatttt atatctgggg tctagaaaag gagttaatct gttttccctc ataaattcac 300  
c 301

<210> 304  
<211> 301  
<212> DNA  
<213> Homo sapien

<400> 304  
acatggatgt tatitttgag actgtcaacc tgaatttgta tttgcttgac attgcctaatt 60  
tattagtttc agtttcagct taccactttt ttgtctgcaa catgcaraas agacagtgcc 120  
cttttttagtg tatcatatca ggaatcatct cacattgggt tgtgccatta ctgggtgcagt 180  
gactttcagc cacttgggta aggtggagtt ggccatatgt ctccactgca aaattactga 240  
ttttcctttt gtaattaata agtgtgtgtg tgaagattct ttgagatgag gtatatatct 300  
c 301

<210> 305  
<211> 301  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(301)  
<223> n = A,T,C or G

<400> 305  
gangtacagc gtggtcaagg taacaagaag aaaaaaatgt gaggggcatc ctgggatgag 60  
caggggggaca gacctggaca gacacgttgt catttgctgc tgtgggtagg aaaatgggag 120  
taaaggagga gaaacagata caaaatctcc aactcagtat taaggatttc tcatgcctag 180  
aatattggta gaaacaagaa tacattcata tggcaaataa ctaaccatgg tggaaacaaa 240  
ttctgggatt taagttggat accaangaaa ttgtattaaa agagctgttc atggaataag 300  
a 301

<210> 306  
<211> 8  
<212> PRT  
<213> Homo sapien

<400> 306  
Val Leu Gly Trp Val Ala Glu Leu

1

5

<210> 307  
<211> 637  
<212> DNA  
<213> Homo sapien

&lt;400&gt; 307

acagggratg	aagggaagagg	gagaggatga	ggaagccccc	ctggggattt	ggtttggtcc	60
ttgtgatcag	gtggtctatg	ggccttatcc	ctacaaagaa	gaatccagaa	ataggggcac	120
attgaggaat	gatacttgag	cccaaagagc	attcaatcat	tgttttattt	gccttmtttt	180
cacaccattg	gtgagggagg	gattaccaac	ctgggggttat	gaagatggtt	gaacacccca	240
cacatagcac	cggagatatg	agatcaacag	tttcttagcc	atagagattc	acagcccaga	300
gcaggaggac	gcttgccacac	catgcaggat	gacatggggg	atgcgctcgg	gattgggtgtg	360
aagaagcaag	gactgttaga	ggcaggcttt	atagtaacaa	gacggtgggg	caaactctga	420
tttccgtggg	ggaatgtcat	ggtcttgctt	tactaagttt	tgagactggc	aggtagtgaa	480
actcattagg	ctgagaacct	tgtggaatgc	acttgaccca	sctgatagag	gaagtagcca	540
ggtgggagcc	tttcccagtg	ggtgtgggac	atatctggca	agattttgtg	gcactcctgg	600
ttacagatac	tggggcagca	aataaaaactg	aatcttg			637

<210> 308  
<211> 647  
<212> DNA  
<213> Homo sapien

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1) ... (647)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 308

acgattttca	ttatcatgta	aatcgggtca	ctcaaggggc	caaccacagc	tgggagccac	60
tgctcagggg	aagggtcata	tgggactttc	tactgcccaa	ggttctatac	aggatataaa	120
ggngcctcac	agtatagatc	tggtagcaaa	gaagaagaaa	caaacactga	tctctttctg	180
ccaccctctt	gacccttttg	aactcctctg	accctttaga	acaagcctac	ctaatactgt	240
ctagagaaaa	gaccaacaac	ggcctcaaag	gatctcttac	catgaaggtc	tcagctaatt	300
cttggtctaag	atgtgggttc	cacattaggt	tctgaatatg	gggggaaggg	tcaatttgct	360
cattttgtgt	gtggataaag	tcaggatgcc	cagggggccag	agcagggggc	tgcttgcttt	420
gggaacaatg	gctgagcata	taaccatagg	ttatggggaa	caaaacaaca	tcaaagtcac	480
tgtatcaatt	gcatgaaga	cttgagggac	ctgaatctac	cgattcatct	taaggcagca	540
ggaccagttt	gagtggcaac	aatgcagcag	cagaatcaat	ggaaacaaca	gaatgattgc	600
aatgtccttt	tttttctcct	gcttctgact	tgataaaagg	ggaccgt		647

<210> 309  
<211> 460  
<212> DNA  
<213> Homo sapien

&lt;400&gt; 309

actttatagt	ttaggctgga	cattggaaaa	aaaaaaaaagc	cagaacaaca	tgtgatagat	60
aatatgattg	gttgccact	tccagactga	tgaatgatga	acgtgatgga	ctattgtatg	120
gagcacatct	tcagcaagag	ggggaaatac	tcatcatttt	tggccagcag	ttgtttgatc	180
accaaaccatc	atgccagaat	actcagcaaa	ccttcttagc	tcttgagaag	tcaaagtcag	240
gggaatttta	ttcctggcaa	ttttaattgg	actccttatg	tgagagcagc	ggctacccag	300
ctggggtggt	ggagcgaacc	cgtcactagt	ggacatgcag	tggcagagct	cctggtaacc	360
acctagagga	atacacaggc	acatgtgtga	tgccaagcgt	gacacctgta	gcactcaaat	420
ttgtcttggt	tttgtctttc	ggtgtgtaag	attcttaagt			460

<210> 310  
<211> 539  
<212> DNA  
<213> Homo sapien

&lt;400&gt; 310

acgggactta	tcaaataaag	ataggaaaag	aagaaaactc	aaatattata	ggcagaaatg	60
ctaaagggtt	taaaatatgt	caggattgga	agaaggcatg	gataaagaac	aaagttcagt	120
taggaaagag	aaacacagaa	ggaagagaca	caataaaaagt	cattatgtat	tctgtgagaa	180
gtcagacagt	aagatttgtg	ggaaatgggt	tggtttgttg	tatggtatgt	attttagcaa	240
taatctttat	ggcagagaaa	gctaaaatcc	tttagcttgc	gtgaatgatc	acttgctgaa	300
ttcctcaagg	taggcatgat	gaaggagggt	ttagaggaga	cacagacaca	atgaactgac	360
ctagatagaa	agccttagta	tactcagcta	ggaatagtga	ttctgagggc	acactgtgac	420
atgattatgt	cattacatgt	atggtagtga	tggggatgat	aggaaggaag	aacttatggc	480
atattttcac	ccccacaaaa	gtcagttaaa	tattgggaca	ctaaccatcc	aggtcaaga	539

&lt;210&gt; 311

&lt;211&gt; 526

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(526)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 311

caaatttgag	ccaatgacat	agaattttac	aaatcaagaa	gcttattctg	gggccatttc	60
ttttgacgtt	ttctctaaac	tactaaagag	gcattaatga	tccataaatt	atattatcta	120
catttacagc	atttaaaatg	tggtcagcat	gaaatattag	ctacagggga	agctaaataa	180
attaacatg	gaataaagat	ttgtccttaa	atataatcta	caagaagact	ttgatatttg	240
tttttcacaa	gtgaagcatt	cttataaagt	gtcataacct	ttttggggaa	actatgggaa	300
aaaatgggga	aactctgaag	ggttttaagt	atcttacctg	aagctacaga	ctccataacc	360
tctctttaca	gggagctcct	gcagccccta	cagaaatgag	tggtctgagt	tcttgattgc	420
acagcaagag	cttctcatct	aaaccctttc	cctttttagt	atctgtgtat	caagtataaa	480
agttctataa	actgtagtnt	acttatttta	atccccaaag	cacagt		526

&lt;210&gt; 312

&lt;211&gt; 500

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(500)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 312

cctctctctc	cccacccct	gactctagag	aactgggttt	tctcccagta	ctccagcaat	60
tcattttctga	aagcagttga	gccactttat	tccaaagtac	actgcagatg	ttcaaactct	120
ccattttctct	ttcccttcca	cctgccagtt	ttgtgactc	tcaacttgct	atgagtgtaa	180
gcattaagga	cattatgctt	cttcgattct	gaagacaggc	cctgctcatg	gatgactctg	240
gcttcttagg	aaaatatttt	tcttccaaaa	tcagtaggaa	atctaaactt	atccctctt	300
tgcatagtgc	tagcagcttc	agacatttgg	ttaagaaccc	atgggaaaaa	aaaaaatcct	360
tgctaattgtg	gtttcctttg	taaaccanga	ttcttatttg	nctggtatag	aatatcagct	420
ctgaacgtgt	ggtaaagatt	tttgtgtttg	aatataggag	aatcagttt	gctgaaaagt	480
tagtcttaat	tatctattgg					500

&lt;210&gt; 313

&lt;211&gt; 718

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(718)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 313

ggagatttgt	gtggtttgca	gccgagggag	accaggaaga	tctgcatggt	gggaaggacc	60
tgatgataca	gaggtgagaa	ataagaaagg	ctgctgactt	taccatctga	ggccacacat	120
ctgctgaaat	ggagataatt	aacatcacta	gaaacagcaa	gatgacaata	taatgtctaa	180
gtagtgacat	gtttttgcac	atttccagcc	cttttaaata	tccacacaca	caggaaagcac	240
aaaaggaagc	acagagatcc	ctgggagaaa	tgcccggccg	ccatcttggg	tcacgatga	300
gcctcgccct	gtgcctgntc	ccgcttggtg	gggaaggaca	ttagaaaatg	aattgatgtg	360
ttccttaaag	gatggcagga	aaacagatcc	tggttggtgat	atttatttga	acgggattac	420
agatttgaag	tgaagtcaca	aagtgaagcat	taccaatgag	aggaaaacag	acgagaaaat	480
cttgatgggt	cacaagacat	gcaacaaaca	aatggaata	ctgtgatgac	acgagcagcc	540
aactggggag	gagataccac	ggggcagagg	tcaggattct	ggccctgctg	cctaactgtg	600
cggtatacca	atcatttcta	tttctaccct	caaacaagct	gtngaataac	tgacttacgg	660
ttctnttggc	ccacattttc	atnatccacc	ccntcntttt	aannttantc	caaantgt	718

&lt;210&gt; 314

&lt;211&gt; 358

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 314

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&lt;210&gt; 315

&lt;211&gt; 341

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 315

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tagcttctgc	tgtaagaggg	tggtgtcccg	ggggctcgtg	cggttattgg	tcctgggctt	300
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&lt;210&gt; 316

&lt;211&gt; 151

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 316

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cattcaggga	gctctggttg	caatattagt	t			151

&lt;210&gt; 317

&lt;211&gt; 151

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 317

agaactagtg	gatcctaagt	aaatacctga	aacatatatt	ggcatttatc	aatggctcaa	60
atcttcattt	atctctggcc	ttaaccttgg	ctcctgaggc	tgccggccagc	agatcccagg	120
ccagggctct	gttcttgcca	cacctgcttg	a			151

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<211> 151  
<212> DNA  
<213> Homo sapien

<400> 318  
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<211> 151  
<212> DNA  
<213> Homo sapien

<400> 319  
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taagattggg tttatgtgat tttagtgggt a 151

<210> 320  
<211> 150  
<212> DNA  
<213> Homo sapien

<400> 320  
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gagcggctgc cttttttttt tttttttttg ggggggaatt tttttttttt aatagttatt 120  
gagtgttcta cagcttacag taaataccat 150

<210> 321  
<211> 151  
<212> DNA  
<213> Homo sapien

<400> 321  
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tgcctctgag aaatcaaagt cttcatacac t 151

<210> 322  
<211> 151  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature  
<222> (1)...(151)  
<223> n = A, T, C or G

<400> 322  
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tttgggcttg gtcagtttgc cacagggctt ggagatgggt acagtcttct ggcattcggc 120  
attgtgcagg gctcgttca nacttcagtt t 151

<210> 323  
<211> 151  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc\_feature

&lt;222&gt; (1)...(151)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 323

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nagactcant	tactaccag	tttgtggtt	twtgaggaa	atgtaactg	acagttagct	120
gttcaatyaa	aaagacactt	ancccatgtg	g			151

&lt;210&gt; 324

&lt;211&gt; 461

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc feature

&lt;222&gt; (1)...(461)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 324

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gccaccatgc	accatggcat	gccagagttc	aacactgttg	ctcttgaaaa	ttgggtctga	420
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&lt;210&gt; 325

&lt;211&gt; 400

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 325

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&lt;210&gt; 326

&lt;211&gt; 1215

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 326

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aaaaaaaaa aaaaaa 1215

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<210> 327  
 <211> 220  
 <212> PRT  
 <213> Homo sapien

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<400> 327
Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met
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Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val
20 25 30
Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly
35 40 45
Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu
50 55 60
Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala
65 70 75 80
Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp
85 90 95
Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn
100 105 110
Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro
115 120 125
Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys
130 135 140
Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly
145 150 155 160
Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro
165 170 175
Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala
180 185 190
Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys
195 200 205
Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
210 215 220

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<210> 328  
 <211> 234  
 <212> DNA  
 <213> Homo sapien

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<400> 328
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agccctggca ggcggcactg gtcattgaaa acgaattggt ctgctcgggc gtcctggtgc 120
atccgcagtg ggtgctgtca gccacacact gtttcagaa ctcctacacc atcgggctgg 180
gcctgcacag tcttgaggcc gaccaagagc caggagacca gatggtggag gcca 234

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<210> 329  
 <211> 77  
 <212> PRT  
 <213> Homo sapien

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<400> 329
Leu Val Ser Gly Ser Cys Ser Gln Ile Ile Asn Gly Glu Asp Cys Ser
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Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu  
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 Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Thr  
                   35                  40                  45  
 His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu  
                   50                  55                  60  
 Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala  
   65                  70                  75

<210> 330  
 <211> 70  
 <212> DNA  
 <213> Homo sapien

<400> 330  
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 gctgcagcca

60  
 70

<210> 331  
 <211> 22  
 <212> PRT  
 <213> Homo sapien

<400> 331  
 Gln His Asn Gly Pro Ile Pro Ser Leu Thr Pro Pro Ser Gly Ser Leu  
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 Val Ser Gly Ser Cys Ser  
                   20

<210> 332  
 <211> 2507  
 <212> DNA  
 <213> Homo sapien

<400> 332  
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 tcgggaagga gacagccaaa gagctggctc agagaggagc tcgagtatat ttagcttgcc 240  
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 gcttcttagc tgaggaaaag cacctccacg tttgatcaa caatgcagga gtgatgatgt 420  
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&lt;210&gt; 333

&lt;211&gt; 3030

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 333

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<210> 334  
 <211> 2417  
 <212> DNA  
 <213> Homo sapien

<400> 334						
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<210> 335  
 <211> 2984

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 335

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&lt;210&gt; 336

&lt;211&gt; 147

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 336

Pro Ser Phe Pro Thr Leu Leu Ser Arg Arg His Leu Gly Ser Tyr Leu

102

```

1           5           10           15
Leu Asp Ser Glu Asn Thr Ser Gly Ala Leu Pro Arg Leu Pro Gln Thr
20           25           30
Pro Lys Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln
35           40           45
Val Ile Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala
50           55           60
Pro Glu Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln
65           70           75           80
Val Lys Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln
85           90           95
Leu Ser Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala
100          105          110
Leu Lys Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn
115          120          125
Ser Tyr Pro Tyr Tyr Pro Tyr Leu Tyr Cys Val Gly Ser Trp Ser Pro
130          135          140
Ala Phe Trp
145

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<210> 337
<211> 9
<212> PRT
<213> Homo sapien

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<400> 337
Ala Leu Thr Gly Phe Thr Phe Ser Ala
1           5

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<210> 338
<211> 9
<212> PRT
<213> Homo sapien

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1           5

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<210> 339
<211> 318
<212> PRT
<213> Homo sapien

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<400> 339
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20           25           30
Cys Thr Ser Thr Val Gln Leu Pro Gly Lys Val Val Val Val Thr Gly
35           40           45
Ala Asn Thr Gly Ile Gly Lys Glu Thr Ala Lys Glu Leu Ala Gln Arg
50           55           60
Gly Ala Arg Val Tyr Leu Ala Cys Arg Asp Val Glu Lys Gly Glu Leu
65           70           75           80
Val Ala Lys Glu Ile Gln Thr Thr Thr Gly Asn Gln Gln Val Leu Val
85           90           95
Arg Lys Leu Asp Leu Ser Asp Thr Lys Ser Ile Arg Ala Phe Ala Lys
100          105          110
Gly Phe Leu Ala Glu Glu Lys His Leu His Val Leu Ile Asn Asn Ala
115          120          125
Gly Val Met Met Cys Pro Tyr Ser Lys Thr Ala Asp Gly Phe Glu Met

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130	135	140
His Ile Gly Val Asn His Leu Gly His Phe Leu Leu Thr His Leu Leu		
145	150	155
Leu Glu Lys Leu Lys Glu Ser Ala Pro Ser Arg Ile Val Asn Val Ser		
	165	170
Ser Leu Ala His His Leu Gly Arg Ile His Phe His Asn Leu Gln Gly		
	180	185
Glu Lys Phe Tyr Asn Ala Gly Leu Ala Tyr Cys His Ser Lys Leu Ala		
	195	200
Asn Ile Leu Phe Thr Gln Glu Leu Ala Arg Arg Leu Lys Gly Ser Gly		
	210	215
Val Thr Thr Tyr Ser Val His Pro Gly Thr Val Gln Ser Glu Leu Val		
225	230	235
Arg His Ser Ser Phe Met Arg Trp Met Trp Trp Leu Phe Ser Phe Phe		
	245	250
Ile Lys Thr Pro Gln Gln Gly Ala Gln Thr Ser Leu His Cys Ala Leu		
	260	265
Thr Glu Gly Leu Glu Ile Leu Ser Gly Asn His Phe Ser Asp Cys His		
	275	280
Val Ala Trp Val Ser Ala Gln Ala Arg Asn Glu Thr Ile Ala Arg Arg		
	290	295
Leu Trp Asp Val Ser Cys Asp Leu Leu Gly Leu Pro Ile Asp		
305	310	315

<210> 340  
 <211> 483  
 <212> DNA  
 <213> Homo sapien

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<210> 341  
 <211> 344  
 <212> DNA  
 <213> Homo sapien

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gctgccttac aagtattaaa tattttactt ctttccataa agagtagctc aaaatatgca	180
attaatttaa taatttctga tgatggtttt atctgcagta atatgtatat catctattag	240
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<210> 342  
 <211> 592  
 <212> DNA  
 <213> Homo sapien

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cctggcaggt aaaccaatgc caagagagt atggaaacca ttggcaagac tttgttgatg	180

104

accaggattg	gaattttata	aaaatattgt	tgatgggaag	ttgctaaagg	gtgaattact	240
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&lt;210&gt; 343

&lt;211&gt; 382

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 343

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&lt;210&gt; 344

&lt;211&gt; 536

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 344

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&lt;210&gt; 345

&lt;211&gt; 251

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 345

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gtgccatttc	c					251

&lt;210&gt; 346

&lt;211&gt; 282

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(282)

&lt;223&gt; n = A, T, C or G

&lt;400&gt; 346

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<210> 347  
 <211> 201  
 <212> DNA  
 <213> Homo sapien  
  
 <220>  
 <221> misc\_feature  
 <222> (1)...(201)  
 <223> n = A,T,C or G

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<210> 348  
 <211> 251  
 <212> DNA  
 <213> Homo sapien

<400> 348						
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<210> 349  
 <211> 251  
 <212> DNA  
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<210> 350  
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 <212> DNA  
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aatcgacg						908

<210> 351  
 <211> 472  
 <212> DNA  
 <213> Homo sapien

<400> 351						
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gtcaaacctt	aatgccattg	ttattgtgaa	ttaggattaa	gtagtaattt	tcaaaattca	120
cattaacttg	attttaaaat	cagwtttgyg	agtcattttac	cacaagctaa	atgtgtacac	180
tatgataaaa	acaaccattg	tattcctgtt	tttctaaaca	gtcctaattt	ctaactgt	240
atatatcctt	cgacatcaat	gaactttgtt	ttcttttact	ccagtaataa	agtaggcaca	300
gatctgtcca	caacaaactt	gccctctcat	gccttgctc	tcacatgct	ctgctccagg	360
tcagccccct	tttgccctgt	ttgttttgtc	aaaaacctaa	tctgcttctt	gcttttcttg	420
gtaatatata	tttagggaag	atgttgcttt	gcccacacac	gaagcaaagt	aa	472

<210> 352  
 <211> 251  
 <212> DNA  
 <213> Homo sapien

<400> 352						
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tgtggataag	gccaggtcaa	tggtgcaag	catgcagaga	aagaggtaca	tcggagcgtg	120
cagggtgcgt	tccgtcctta	cgatgaagac	cacgatgcag	tttccaaaca	ttgccactac	180
atacatggaa	aggaggggga	agccaaccca	gaaatgggct	ttctctaate	ctgggataacc	240
aataagcaca	a					251

<210> 353  
 <211> 436  
 <212> DNA  
 <213> Homo sapien

<400> 353						
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cacattatgg	tattattact	atactgatta	tatttatcat	gtgacttcta	attaraaaat	120
gtatccaaaa	gcaaaacagc	agatatacaa	aattaaagag	acagaagata	gacattaaca	180
gataaggcaa	cttatacatt	gacaatccaa	atccaatata	tttaaacatt	tgaggaaatga	240
gggggacaaa	tggaagccar	atcaaatttg	tgtaaaacta	ttcagtatgt	ttcccttgct	300
tcatgtctga	raaggctctc	ccttcaatgg	ggatgacaaa	ctccaaatgc	cacacaaatg	360
ttaacagaat	actagattca	cactggaacg	ggggtaaaga	agaaattatt	ttctataaaa	420
gggtccttaa	tgtagt					436

<210> 354  
 <211> 854  
 <212> DNA  
 <213> Homo sapien

<400> 354						
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caagtctgaa	accaaactca	ggaaacatag	gaaacgagcc	aggcacaggg	ctggtgggcc	120
atcagggacc	accctttggg	ttgatatttt	gcttaatctg	catcttttga	gtaagatcat	180
ctgggcagtag	aagctgttct	ccagggtacat	ttctctagct	catgtacaaa	aacatcctga	240
aggactttgt	caggtgcctt	gctaaaagcc	agatgcgttc	ggcacttcct	tggtctgagg	300
ttaattgcac	acctacaggc	actgggctca	tgttttcaag	tattttgtcc	tcactttagg	360
gtgagtga	gatccccatt	ataggagcac	ttgggagaga	tcataataaa	gctgactctt	420
gagtacatgc	agtaatggg	tagatgtgtg	tggtgtgtct	tcattcctgc	aagggtgctt	480



107

gttagggagt	gtttccagga	ggaacaagtc	tgaaccaat	catgaaataa	atggtaggtg	540
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caatatggaa	ggctctaatt	tgcccatatt	tgaataata	attcagcttt	ttgtaataca	660
aaataacaaa	ggattgagaa	tcatggtgtc	taatgtataa	aagaccagg	aaacataaat	720
atatcaactg	cataaatgta	aaatgcatgt	gacccaagaa	ggcccaaaag	tggcagacaa	780
cattgtaccc	attttccctt	ccaaaatgtg	agcggcgggc	ctgctgcttt	caaggctgtc	840
acacgggatg	tcag					854

<210> 355  
 <211> 676  
 <212> DNA  
 <213> Homo sapien

<400> 355						
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cagggtcaaag	ctgatctttc	tggaatgtca	ccaaccaagg	gcctatatatt	atcaaaagcc	120
atccacaagt	catacctgga	tgtcagcgaa	gagggcacgg	aggcagcagc	agccactggg	180
gacagcatcg	ctgtaaaaaag	cctaccaatg	agagctcagt	tcaaggcgaa	ccacccttct	240
ctgttcttta	taaggcacac	tcataccaac	acgatcctat	tctgtggcaa	gcttgcctct	300
ccctaatacag	atggggttga	gtaaggctca	gagttgcaga	tgaggtgcag	agacaatcct	360
gtgactttcc	cacggccaaa	aagctgttca	cacctcacgc	acctctgtgc	ctcagtttgc	420
tcatctgcaa	aataggtcta	ggatttcttc	caaccatttc	atgagttgtg	aagctaaggc	480
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ggtgtctcat	ttgagtgctg	tccagtgaca	tgatcaagtc	aatgagtaaa	attttaaggg	600
attagatttt	cttgacttgt	atgtatctgt	gagatcttga	ataagtgacc	tgacatctct	660
gcttaaagaa	aaccag					676

<210> 356  
 <211> 574  
 <212> DNA  
 <213> Homo sapien

<400> 356						
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caagcttccc	atttgtagat	ctcagtgccct	atgagtatct	gacacctgtt	cctctcttca	180
gtctcttagg	gaggcttaaa	tctgtctcag	gtgtgctaag	agtgccagcc	caaggkgttc	240
aaaagtccac	aaaactgcag	tctttgtctg	gatagtaagc	caagcagtcg	ctggacagca	300
gagttctttt	cttgggcaac	agataaccag	acaggactct	aatcgtgctc	ttattcaaca	360
ttcttctgtc	tctgcctaga	ctggaataaa	aagccaatct	ctctcgtggc	acaggggaagg	420
agatacaagc	tcgtttacat	gtgatagatc	taacaaaggc	atctaccgaa	gtctggtctg	480
gatagacggc	acagggagct	cttaggtcag	cgctgctggg	tggaggacat	tcctgagtc	540
agctttgcag	cctttgtgca	acagtacttt	ccca			574

<210> 357  
 <211> 393  
 <212> DNA  
 <213> Homo sapien

<400> 357						
tttttttttt	tttttttttt	tttttttttt	tacagaatat	aratgcttta	tcactgkact	60
taatattgkg	kcttggtcac	tatacttaaa	aatgcaccac	tcataaatat	ttaattcagc	120
aagccacaac	caaracttga	ttttatcaac	aaaaaccctt	aatataaac	ggsaaaaaag	180
atagatataa	ttattccagt	ttttttaaaa	cttaaaarat	attccattgc	cgaatttaara	240
araarataag	tggttatatg	aaagaagggc	attcaagcac	actaaaraaa	cctgaggkaa	300
gcataatctg	tacaaaatta	aactgtcctt	tttggcattt	taacaaattt	gcaacgktct	360
tttttttctt	tttctgtttt	tttttttttt	tac			393

<210> 358  
 <211> 630  
 <212> DNA  
 <213> Homo sapien

<400> 358  
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ttaatgttta taggaaaatg atgagtttat gacaaaggaa gtagatagtg ttttacaaga 120  
gcatagagta gggaagctaa tccagcacag ggaggtcaca gagacatccc taaggaagtg 180  
gagtttaaac tgagagaagc aagtgcctaa actgaaggat gtgttgaaga agaagggaga 240  
gtagaacaat ttgggcagag ggaaccttat agaccctaag gtgggaaggt tcaaagaact 300  
gaaagagagc tagaacagct ggagccgttc tccggtgtaa agaggagtca aagagataag 360  
attaaagatg tgaagattaa gatcttggtg gcattcaggg attggcactt ctacaagaaa 420  
tcactgaagg gagtaatgtg acattacttt tcaacttcagg atggccattc taactccagg 480  
gggtagactg gactaggtaa gactggaggc aggtagacct cttctaaggc ctgcgatagt 540  
gaaagacaaa aataagtggg gaaattcagg ggtagtgaa aatcagtagg acttaatgag 600  
caagccagag gttcctccac aacaaccagt 630

<210> 359  
<211> 620  
<212> DNA  
<213> Homo sapien

<400> 359  
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ctcaccagaa gaataaagtg ctctgccagt tattaaggga ttactgctgg tgaattaaat 180  
atggcattcc ccaagggaaa tagagagatt cttctggatt atgttcaata tttatttcac 240  
aggattaact gttttaggaa cagatataaa gcttcgccac ggaagagatg gacaaagcac 300  
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tgcaacatta tgcttcatga ataatatgta gaaagaaggt ctgatgaaaa tgacatcctt 420  
aatgtaagat aactttataa gaattctggg tcaaataaaa ttctttgaag aaaacatcca 480  
aatgtcattg acttatcaaa tactatcttg gcatataacc tatgaaggca aaactaaaca 540  
aacaanaagc tcacaccaa caaaaccatc aacttatttt gtattctata acatacgaga 600  
ctgtaagat gtgacagtgt 620

<210> 360  
<211> 431  
<212> DNA  
<213> Homo sapien

<400> 360  
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tgatgaatga tgaacgtgat ggactattgt atggagcaca tcttcagcaa gagggggaaa 120  
tactcatcat ttttgccag cagttgtttg atcaccaaaac atcatgccag aatactcagc 180  
aaaccttctt agctcttgag aagtcaaaagt ccgggggaat ttattcctgg caattttaat 240  
tggaactcctt atgtgagagc agcggctacc cagctggggt ggtggagcga acccgctact 300  
agtggacatg cagtggcaga gtcctggta accacctaga ggaatacaca ggcaatgtg 360  
tgatgccaaag cgtgacacct gtagcactca aatttgtctt gtttttgtct ttcgggtgtg 420  
agattcttag t 431

<210> 361  
<211> 351  
<212> DNA  
<213> Homo sapien

<400> 361  
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ttgacttctt ccggggcttt cccgagggct tcaccgtgag ccctgcggcc ctgagggctg 240  
caatcctgga ttcaatgtct gaaacctcgc tctctgcctg ctggacttct gaggccgtca 300  
ctgccactct gtcctccagc tctgacagct cctcatctgt ggtcctgttg t 351

<210> 362  
<211> 463

<212> DNA  
<213> Homo sapien

<400> 362  
acttcatcag gccataatgg gtgcctcccg tgagaatcca agcacctttg gactgcgcga 60  
tgtatagatgag ccggctgaag atctttgcgca tgcgcggcct cagggcgaag ttcttggcgc 120  
ccccggtcac agaaatgacc aggttgggtg ttttcagggt ccagtgcctg gtcagcagct 180  
cgtaaaggat ttccgcgtcc gtgtcgcagg acagacgtat atacttccct ttcttcccca 240  
gtgtctcaaa ctgaatatcc ccaaaggcgt cggtaggaaa ttccttgggtg tgtttcttgt 300  
agttccattt ctcacttttg ttgatctggg tgccttccat gtgctggctc tgggcatagc 360  
cacacttgca cacattctcc ctgataagca cgatggtgtg gacaggaagg aaggatttca 420  
ttgagcctgc ttatggaaac tggatttgtt agcttaaata gac 463

<210> 363  
<211> 653  
<212> DNA  
<213> Homo sapien

<220>  
<221> misc feature  
<222> (1)...(653)  
<223> n = A,T,C or G

<400> 363  
acccccgagt ncctgnctgg catactngga acgaccaacg acacacccaa gctcggcctc 60  
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tgaggaggcac tacgcaagat gggactgcgt cctgggggtga gacatcctct ccttggagat 180  
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tagcaagatg naagtgttga gantcattgc agaggttcag aaaagagacc cntcgtgact 360  
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ntgggccctg tagctgggat gacattgagt ttgagctgct gacctgggat gaggaaggag 540  
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cccgcctccag attccctcag acctttgccc gtcccattat tggctcstggt ggt 653

<210> 364  
<211> 401  
<212> DNA  
<213> Homo sapien

<400> 364  
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tgagaaagct caattataga tgcaaagtta taactaaact actatagtag taaagaaata 240  
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acgtgcatag taaatcttta tatttgctat ggcgttgac tagaggactt ggactgcaac 360  
aagtggatgc gcggaaaatg aaatcttctt caatagccca g 401

<210> 365  
<211> 356  
<212> DNA  
<213> Homo sapien

<400> 365  
ccagtgtcat atttgggctt aaaatttcaa gaagggcact tcaaattggct ttgcatttgc 60  
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taccagagca tcaagtctct gcagcaggctc attcttgggt aaagaaatga cttccacaaa 180  
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gactgtcacg atgtgtatag tacagtttga caagcctggg tccatacaga ccgctggaga 300  
acattcggca atgtcccctt tgtagccagt ttcttcttcg agctcccga gagcag 356

110

<210> 366  
 <211> 1851  
 <212> DNA  
 <213> Homo sapien

<400> 366  
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 tcacttcctt taagcctttg tgactcttcc tctgatgtca gctttaagtc ttgttctgga 180  
 ttgctgtttt cagaagagat ttttaacatc tgtttttctt tgtagtcaga aagtaactgg 240  
 caaattacat gatgatgact agaaacagca tactctctgg ccgtctttcc agatcttgag 300  
 aagatacatc aacattttgc tcaagtagag ggctgactat acttgctgat ccacaacata 360  
 cagcaagtat gagagcagtt cttccatatac tatccagcgc atttaaattc gcttttttct 420  
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 gcaagagttt tactacttct gaattcccat tggcagagggc cagatgtaga gcagtcctct 780  
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 aatataattt tcctctggag ccatatggat gaactatgaa ggaagaactc cccgaagaag 1440  
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 tcacataaaa agaattaaaa gcaaagtcac ataagcatct caacagacac agaaaaggca 1680  
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 cttttcccca tttagtatta tgttggtgt gggcttgtca taggtggtt ttattacttt 1800  
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<210> 367  
 <211> 668  
 <212> DNA  
 <213> Homo sapien

<400> 367  
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 accrtataag agcagtgtt tggccattaa tttatcttcc attrtagaca gcrtagtgya 180  
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 gcagtcctat gagagtgaga agacttttta ggaaattgta gtgcactagc tacagccata 600  
 gcaatgattc atgtaactgc aaacactgaa tagcctgcta ttactctgcc ttcaaaaaaa 660  
 aaaaaaa 668

<210> 368  
 <211> 1512  
 <212> DNA  
 <213> Homo sapien

&lt;400&gt; 368

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gaagtagtaa	aactcstgct	ggacagacga	tgtcaactta	atgtccttga	caacaaaaag	840
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gaaaatattt	tgaatgacc	taattatctm	agactttatt	ttaaattattg	ttattttcaa	1200
agaagcatta	gagggtagac	tttttttttt	ttaaattgac	ttctggtaaa	tacttttggt	1260
gaaaacactg	aatttgtaaa	aggtaatact	tactattttt	caatttttcc	ctcctaggat	1320
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taaaaaacag	taatagatac	gaggtgatgc	gcctgtcagt	ggcaagggtt	aagatatttc	1500
tgatctcgtg	cc					1512

&lt;210&gt; 369

&lt;211&gt; 1853

&lt;212&gt; DNA

&lt;213&gt; Homo sapien

&lt;400&gt; 369

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<210> 370  
 <211> 2184  
 <212> DNA  
 <213> Homo sapien

<400> 370						
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tggatgaaga	gtattacgtt	gtgcagatat	actgcagtgt	cttcactctc	tgatgtgtga	540
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<210> 371  
 <211> 1855  
 <212> DNA  
 <213> Homo sapien

<220>  
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gccgcccccg	cataaccgtc	agactggcct	gtaacggctt	gcaggcgac	gccgcacgcg	180
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tcgcgttct	ttgctggact	tgacctttty	tctgctgggt	ttggcattcc	tttggggtgg	420
gctgggtgtt	ttctccggg	gggkktgccc	ttctgggggt	gggctgggk	cgccccagg	480
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<210> 372  
 <211> 1059  
 <212> DNA  
 <213> Homo sapien

<400> 372						
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<210> 373  
 <211> 1155  
 <212> DNA  
 <213> Homo sapien

<400> 373						
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gccagagagt	atgctgtttc	tagtcatcat	catgtaattt	gccagttact	ttctgactac	1080
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<210> 374  
 <211> 2000  
 <212> DNA  
 <213> Homo sapien

<400> 374						
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aaaaaaaaaa	aaaaaaaaaa					2000

<210> 375



<211> 2040  
 <212> DNA  
 <213> Homo sapien

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 agcaacgtgg gcacttctgg agaccacgac gactctgcta tgaagacact caggagcaag 180  
 atgggcaagt ggtgccgcca ctgcttcccc tgctgcaggg ggagtggcaa gagcaactg 240  
 ggcgcttctg gagaccacga cgactctgct atgaagacac tcaggaacaa gatgggcaag 300  
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 aagcaatttt gtgaagaaca gaacactgga atattacacg atgagattct gattcatgaa 1860  
 gaaaagcaga tagaagtggg tgaaaaaatg aattctgagc tttctcttag ttgtaagaaa 1920  
 gaaaaagaca tcttgcatga aaatagtacg ttgcgggaag aaattgccat gctaagactg 1980  
 gagctagaca caatgaaaca tcagagccag ctaaaaaaa aaaaaaaaaa aaaaaaaaaa 2040

<210> 376  
 <211> 329  
 <212> PRT  
 <213> Homo sapien

<400> 376  
 Met Asp Ile Val Val Ser Gly Ser His Pro Leu Trp Val Asp Ser Phe  
 1 5 10 15  
 Leu His Leu Ala Gly Ser Asp Leu Leu Ser Arg Ser Leu Met Ala Glu  
 20 25 30  
 Glu Tyr Thr Ile Val His Ala Ser Phe Ile Ser Cys Ile Ser Ser Ser  
 35 40 45  
 Leu Asp Gly Gln Gly Glu Arg Gln Glu Gln Arg Gly His Phe Trp Arg  
 50 55 60  
 Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Glu Val Gln Val  
 65 70 75 80  
 Val Leu Pro Leu Leu Pro Leu Leu Gln Gly Ser Gly Lys Ser Asn Val  
 85 90 95  
 Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr  
 100 105 110  
 His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp  
 115 120 125

116

Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp  
 130 135 140  
 Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser  
 145 150 155 160  
 Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys  
 165 170 175  
 Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala  
 180 185 190  
 Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly  
 195 200 205  
 Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr  
 210 215 220  
 Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr  
 225 230 235 240  
 Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu  
 245 250 255  
 Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys  
 260 265 270  
 Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu  
 275 280 285  
 Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu  
 290 295 300  
 Glu Gln Asn Val Asp Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu  
 305 310 315 320  
 Ser Met Leu Phe Leu Val Ile Ile Met  
 325

&lt;210&gt; 377

&lt;211&gt; 148

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;220&gt;

&lt;221&gt; VARIANT

&lt;222&gt; (1)...(148)

&lt;223&gt; Xaa = Any Amino Acid

&lt;400&gt; 377

Met Thr Xaa Pro Ser Trp Ser Pro Gly Thr Thr Ser Val Glu Lys Ile  
 1 5 10 15  
 Trp Thr Ser Ser Thr Glu Leu Pro Trp Trp Gly Lys Val Pro Arg Lys  
 20 25 30  
 Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Xaa Asp Lys  
 35 40 45  
 Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu  
 50 55 60  
 Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp  
 65 70 75 80  
 Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp  
 85 90 95  
 Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro  
 100 105 110  
 Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp  
 115 120 125  
 Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser  
 130 135 140  
 Lys Asn Lys Val  
 145

&lt;210&gt; 378

&lt;211&gt; 1719

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 378

Met	Val	Val	Glu	Val	Asp	Ser	Met	Pro	Ala	Ala	Ser	Ser	Val	Lys	Lys
1				5					10					15	
Pro	Phe	Gly	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp	Cys	Cys	Arg	Cys	Phe
			20					25					30		
Pro	Cys	Cys	Arg	Glu	Ser	Gly	Lys	Ser	Asn	Val	Gly	Thr	Ser	Gly	Asp
		35					40					45			
His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp
	50					55					60				
Cys	Arg	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser	Gly	Lys	Ser	Asn	Val
65					70					75				80	
Gly	Ala	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Asn
				85					90					95	
Lys	Met	Gly	Lys	Trp	Cys	Cys	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser
			100					105					110		
Gly	Lys	Ser	Lys	Val	Gly	Ala	Trp	Gly	Asp	Tyr	Asp	Asp	Ser	Ala	Phe
		115					120					125			
Met	Glu	Pro	Arg	Tyr	His	Val	Arg	Gly	Glu	Asp	Leu	Asp	Lys	Leu	His
	130					135					140				
Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val	Pro	Arg	Lys	Asp	Leu	Ile	Val	Met
145					150					155				160	
Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys	Gln	Lys	Arg	Thr	Ala
				165					170					175	
Leu	His	Leu	Ala	Ser	Ala	Asn	Gly	Asn	Ser	Glu	Val	Val	Lys	Leu	Leu
		180					185						190		
Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp	Asn	Lys	Lys	Arg	Thr
	195						200					205			
Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp	Glu	Cys	Ala	Leu	Met
	210					215					220				
Leu	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro	Asp	Glu	Tyr	Gly	Asn
225					230					235				240	
Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp	Lys	Leu	Met	Ala	Lys
			245						250					255	
Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser	Lys	Asn	Lys	His	Gly
		260					265						270		
Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val	His	Glu	Gln	Lys	Gln	Gln	Val	Val
		275					280					285			
Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala	Asn	Leu	Asn	Ala	Leu	Asp	Arg	Tyr
	290					295					300				
Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys	Gly	Ser	Ala	Ser	Ile
305					310					315				320	
Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val	Ser	Ser	Gln	Asp	Leu
			325						330					335	
Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser	Ser	His	His	His	Val
			340					345					350		
Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Leu	Lys	Ile
	355						360					365			
Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Asn	Val	Ser	Arg	Thr	Arg	Asn	Lys
	370					375					380				
Pro	Arg	Thr	His	Met	Val	Val	Glu	Val	Asp	Ser	Met	Pro	Ala	Ala	Ser
385					390						395			400	
Ser	Val	Lys	Lys	Pro	Phe	Gly	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp	Cys
			405						410					415	
Cys	Arg	Cys	Phe	Pro	Cys	Cys	Arg	Glu	Ser	Gly	Lys	Ser	Asn	Val	Gly
			420					425					430		
Thr	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Ser	Lys
		435					440					445			
Met	Gly	Lys	Trp	Cys	Arg	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser	Gly
	450					455					460				
Lys	Ser	Asn	Val	Gly	Ala	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys

465					470					475				480
Thr	Leu	Arg	Asn	Lys	Met	Gly	Lys	Trp	Cys	Cys	His	Cys	Phe	Pro Cys
				485					490					495
Cys	Arg	Gly	Ser	Gly	Lys	Ser	Lys	Val	Gly	Ala	Trp	Gly	Asp	Tyr Asp
			500					505					510	
Asp	Ser	Ala	Phe	Met	Glu	Pro	Arg	Tyr	His	Val	Arg	Gly	Glu	Asp Leu
		515					520					525		
Asp	Lys	Leu	His	Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val	Pro	Arg	Lys Asp
	530					535					540			
Leu	Ile	Val	Met	Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys Gln
545					550					555				560
Lys	Arg	Thr	Ala	Leu	His	Leu	Ala	Ser	Ala	Asn	Gly	Asn	Ser	Glu Val
				565					570					575
Val	Lys	Leu	Leu	Leu	Asp	Arg	Arg	Cys	Gln	Leu	Asn	Val	Leu	Asp Asn
			580					585					590	
Lys	Lys	Arg	Thr	Ala	Leu	Ile	Lys	Ala	Val	Gln	Cys	Gln	Glu	Asp Glu
		595					600					605		
Cys	Ala	Leu	Met	Leu	Leu	Glu	His	Gly	Thr	Asp	Pro	Asn	Ile	Pro Asp
	610					615					620			
Glu	Tyr	Gly	Asn	Thr	Thr	Leu	His	Tyr	Ala	Ile	Tyr	Asn	Glu	Asp Lys
625					630					635				640
Leu	Met	Ala	Lys	Ala	Leu	Leu	Leu	Tyr	Gly	Ala	Asp	Ile	Glu	Ser Lys
				645					650					655
Asn	Lys	His	Gly	Leu	Thr	Pro	Leu	Leu	Leu	Gly	Val	His	Glu	Gln Lys
			660				665						670	
Gln	Gln	Val	Val	Lys	Phe	Leu	Ile	Lys	Lys	Lys	Ala	Asn	Leu	Asn Ala
		675					680					685		
Leu	Asp	Arg	Tyr	Gly	Arg	Thr	Ala	Leu	Ile	Leu	Ala	Val	Cys	Cys Gly
	690					695					700			
Ser	Ala	Ser	Ile	Val	Ser	Leu	Leu	Leu	Glu	Gln	Asn	Ile	Asp	Val Ser
705					710					715				720
Ser	Gln	Asp	Leu	Ser	Gly	Gln	Thr	Ala	Arg	Glu	Tyr	Ala	Val	Ser Ser
				725					730					735
His	His	His	Val	Ile	Cys	Gln	Leu	Leu	Ser	Asp	Tyr	Lys	Glu	Lys Gln
			740				745						750	
Met	Leu	Lys	Ile	Ser	Ser	Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp	Leu Lys
		755					760					765		
Leu	Thr	Ser	Glu	Glu	Glu	Ser	Gln	Arg	Phe	Lys	Gly	Ser	Glu	Asn Ser
	770					775					780			
Gln	Pro	Glu	Lys	Met	Ser	Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp	Gly Asp
785					790					795				800
Arg	Glu	Val	Glu	Glu	Met	Lys	Lys	His	Glu	Ser	Asn	Asn	Val	Gly
				805					810					815
Leu	Leu	Glu	Asn	Leu	Thr	Asn	Gly	Val	Thr	Ala	Gly	Asn	Gly	Asp Asn
			820				825						830	
Gly	Leu	Ile	Pro	Gln	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Asn	Gln	Gln Phe
		835					840					845		
Pro	Asp	Asn	Glu	Ser	Glu	Glu	Tyr	His	Arg	Ile	Cys	Glu	Leu	Val Ser
	850					855					860			
Asp	Tyr	Lys	Glu	Lys	Gln	Met	Pro	Lys	Tyr	Ser	Ser	Glu	Asn	Ser Asn
865					870					875				880
Pro	Glu	Gln	Asp	Leu	Lys	Leu	Thr	Ser	Glu	Glu	Glu	Ser	Gln	Arg Leu
				885					890					895
Glu	Gly	Ser	Glu	Asn	Gly	Gln	Pro	Glu	Leu	Glu	Asn	Phe	Met	Ala Ile
			900				905						910	
Glu	Glu	Met	Lys	Lys	His	Gly	Ser	Thr	His	Val	Gly	Phe	Pro	Glu Asn
		915					920					925		
Leu	Thr	Asn	Gly	Ala	Thr	Ala	Gly	Asn	Gly	Asp	Asp	Gly	Leu	Ile Pro
	930					935					940			
Pro	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Ser	Gln	Gln	Phe	Pro	Asp	Thr Glu
945					950					955				960
Asn	Glu	Glu	Tyr	His	Ser	Asp	Glu	Gln	Asn	Asp	Thr	Gln	Lys	Gln Phe

	965								970							975		
Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His																		
Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser	980								985							990		
Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu	995								1000							1005		
Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His	1010								1015							1020		
Gln Ser Gln Leu Pro Arg Thr His Met Val Val Glu Val Asp Ser Met	1025								1030							1035		
Pro Ala Ala Ser Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met	1045								1050							1055		
Gly Lys Trp Cys Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys	1060								1065							1070		
Ser Asn Val Gly Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr	1075								1080							1085		
Leu Arg Ser Lys Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys	1090								1095							1100		
Arg Gly Ser Gly Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp	1105								1110							1115		
Ser Ala Met Lys Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His	1125								1130							1135		
Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp	1140								1145							1150		
Gly Asp Tyr Asp Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg	1155								1160							1165		
Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val	1170								1175							1180		
Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys	1185								1190							1195		
Lys Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly	1205								1210							1215		
Asn Ser Glu Val Val Lys Leu Leu Leu Asp Arg Arg Cys Gln Leu Asn	1220								1225							1230		
Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys	1235								1240							1245		
Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro	1250								1255							1260		
Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr	1265								1270							1275		
Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp	1285								1290							1295		
Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Val	1300								1305							1310		
His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala	1315								1320							1325		
Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala	1330								1335							1340		
Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn	1345								1350							1355		
Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr	1365								1370							1375		
Ala Val Ser Ser His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr	1380								1385							1390		
Lys Glu Lys Gln Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu	1395								1400							1405		
Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly	1410								1415							1420		
Ser Glu Asn Ser Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn	1425								1430							1435		
Lys Asp Gly Asp Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser	1445								1450							1455		

120

Asn	Asn	Val	Gly	Leu	Leu	Glu	Asn	Leu	Thr	Asn	Gly	Val	Thr	Ala	Gly
	1475						1480					1485			
Asn	Gly	Asp	Asn	Gly	Leu	Ile	Pro	Gln	Arg	Lys	Ser	Arg	Thr	Pro	Glu
	1490						1495					1500			
Asn	Gln	Gln	Phe	Pro	Asp	Asn	Glu	Ser	Glu	Glu	Tyr	His	Arg	Ile	Cys
1505					1510					1515					152
Glu	Leu	Val	Ser	Asp	Tyr	Lys	Glu	Lys	Gln	Met	Pro	Lys	Tyr	Ser	Ser
				1525						1530					1535
Glu	Asn	Ser	Asn	Pro	Glu	Gln	Asp	Leu	Lys	Leu	Thr	Ser	Glu	Glu	Glu
			1540					1545						1550	
Ser	Gln	Arg	Leu	Glu	Gly	Ser	Glu	Asn	Gly	Gln	Pro	Glu	Lys	Arg	Ser
	1555						1560					1565			
Gln	Glu	Pro	Glu	Ile	Asn	Lys	Asp	Gly	Asp	Arg	Glu	Leu	Glu	Asn	Phe
	1570					1575					1580				
Met	Ala	Ile	Glu	Glu	Met	Lys	Lys	His	Gly	Ser	Thr	His	Val	Gly	Phe
1585					1590					1595					160
Pro	Glu	Asn	Leu	Thr	Asn	Gly	Ala	Thr	Ala	Gly	Asn	Gly	Asp	Asp	Gly
				1605					1610						1615
Leu	Ile	Pro	Pro	Arg	Lys	Ser	Arg	Thr	Pro	Glu	Ser	Gln	Gln	Phe	Pro
		1620						1625						1630	
Asp	Thr	Glu	Asn	Glu	Glu	Tyr	His	Ser	Asp	Glu	Gln	Asn	Asp	Thr	Gln
	1635						1640					1645			
Lys	Gln	Phe	Cys	Glu	Glu	Gln	Asn	Thr	Gly	Ile	Leu	His	Asp	Glu	Ile
	1650					1655					1660				
Leu	Ile	His	Glu	Glu	Lys	Gln	Ile	Glu	Val	Val	Glu	Lys	Met	Asn	Ser
1665					1670					1675					168
Glu	Leu	Ser	Leu	Ser	Cys	Lys	Lys	Glu	Lys	Asp	Ile	Leu	His	Glu	Asn
				1685					1690						1695
Ser	Thr	Leu	Arg	Glu	Glu	Ile	Ala	Met	Leu	Arg	Leu	Glu	Leu	Asp	Thr
		1700						1705						1710	
Met	Lys	His	Gln	Ser	Gln	Leu									
					1715										

&lt;210&gt; 379

&lt;211&gt; 656

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 379

Met	Val	Val	Glu	Val	Asp	Ser	Met	Pro	Ala	Ala	Ser	Ser	Val	Lys	Lys
1				5				10						15	
Pro	Phe	Gly	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp	Cys	Cys	Arg	Cys	Phe
			20					25					30		
Pro	Cys	Cys	Arg	Glu	Ser	Gly	Lys	Ser	Asn	Val	Gly	Thr	Ser	Gly	Asp
		35					40					45			
His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Ser	Lys	Met	Gly	Lys	Trp
	50					55					60				
Cys	Arg	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser	Gly	Lys	Ser	Asn	Val
65				70					75					80	
Gly	Ala	Ser	Gly	Asp	His	Asp	Asp	Ser	Ala	Met	Lys	Thr	Leu	Arg	Asn
			85					90						95	
Lys	Met	Gly	Lys	Trp	Cys	Cys	His	Cys	Phe	Pro	Cys	Cys	Arg	Gly	Ser
			100					105					110		
Gly	Lys	Ser	Lys	Val	Gly	Ala	Trp	Gly	Asp	Tyr	Asp	Asp	Ser	Ala	Phe
		115				120						125			
Met	Glu	Pro	Arg	Tyr	His	Val	Arg	Gly	Glu	Asp	Leu	Asp	Lys	Leu	His
	130					135					140				
Arg	Ala	Ala	Trp	Trp	Gly	Lys	Val	Pro	Arg	Lys	Asp	Leu	Ile	Val	Met
145				150						155					160
Leu	Arg	Asp	Thr	Asp	Val	Asn	Lys	Lys	Asp	Lys	Gln	Lys	Arg	Thr	Ala
				165				170							175

Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu  
 180 185 190  
 Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr  
 195 200 205  
 Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met  
 210 215 220  
 Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn  
 225 230 235 240  
 Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys  
 245 250 255  
 Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly  
 260 265 270  
 Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val  
 275 280 285  
 Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr  
 290 295 300  
 Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile  
 305 310 315 320  
 Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu  
 325 330 335  
 Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val  
 340 345 350  
 Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile  
 355 360 365  
 Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu  
 370 375 380  
 Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys  
 385 390 395 400  
 Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu  
 405 410 415  
 Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn  
 420 425 430  
 Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro  
 435 440 445  
 Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu  
 450 455 460  
 Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu  
 465 470 475 480  
 Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp  
 485 490 495  
 Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu  
 500 505 510  
 Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys  
 515 520 525  
 Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly  
 530 535 540  
 Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser  
 545 550 555 560  
 Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr  
 565 570 575  
 His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln  
 580 585 590  
 Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln  
 595 600 605  
 Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys  
 610 615 620  
 Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile  
 625 630 635 640  
 Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu  
 645 650 655

122

<211> 671  
 <212> PRT  
 <213> Homo sapien

<400> 380

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Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
 1      5      10      15
Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
 20      25      30
Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
 35      40      45
His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
 50      55      60
Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
 65      70      75      80
Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
 85      90      95
Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
100      105      110
Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
115      120      125
Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
130      135      140
Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
145      150      155      160
Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
165      170      175
Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
180      185      190
Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
195      200      205
Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
210      215      220
Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
225      230      235      240
Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
245      250      255
Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
260      265      270
Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
275      280      285
Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
290      295      300
Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
305      310      315      320
Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
325      330      335
Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val
340      345      350
Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile
355      360      365
Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu
370      375      380
Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys
385      390      395      400
Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu
405      410      415
Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn
420      425      430
Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro
435      440      445
Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu

```



450  
 Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu  
 465 470 475 480  
 Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp  
 485 490 495  
 Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu  
 500 505 510  
 Asn Gly Gln Pro Glu Lys Arg Ser Gln Glu Pro Glu Ile Asn Lys Asp  
 515 520 525  
 Gly Asp Arg Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys Lys  
 530 535 540  
 His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly Ala  
 545 550 555 560  
 Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser Arg  
 565 570 575  
 Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr His  
 580 585 590  
 Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln Asn  
 595 600 605  
 Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln Ile  
 610 615 620  
 Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys Lys  
 625 630 635 640  
 Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile Ala  
 645 650 655  
 Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu  
 660 665 670

<210> 381  
 <211> 251  
 <212> DNA  
 <213> Homo sapien

<400> 381  
 ggagaagcgt ctgctggggc aggaaggggt ttccctgccc tctcacctgt ccctcaccaa 60  
 ggtaacatgc ttcccctaag ggtatcccaa cccaggggcc tcaccatgac ctctgagggg 120  
 ccaatatccc aggagaagca ttggggaggt gggggcaggt gaaggacca ggactcacac 180  
 atcctgggcc tccaaggcag aggagaggggt cctcaagaag gtcaggagga aaatccgtaa 240  
 caagcagtca g 251

<210> 382  
 <211> 3279  
 <212> DNA  
 <213> Homo sapiens

<400> 382  
 cttctgcag ccccatgct ggtgaggggc acgggcagga acagtggacc caacatggaa 60  
 atgctggagg gtgtcaggaa gtgatcgggc tctggggcag ggaggagggg tggggagtgt 120  
 cactggggagg ggacatcctg cagaaggtag gagttagcaa acaccgctg caggggaggg 180  
 gagagccctg cggcacctgg gggagcagag ggagcagcac ctgcccaggc ctgggaggag 240  
 gggcctggag ggcgtgagga ggagcgaggg ggctgcatgg ctggagttag ggatcagggg 300  
 cagggcgcgga gatggcctca cacagggaag agagggcccc tctgcaggg cctcacctgg 360  
 gccacaggag gacactgctt ttcctctgag gagtacaggag ctgtggatgg tgctggacag 420  
 aagaaggaca gggcctggct cagggtgtcca gaggtgtcg ctggcttccc tttgggatca 480  
 gactgcaggg agggagggcg gcagggttgt ggggggagtg acgatgagga tgacctgggg 540  
 gtggctccag gccttgcccc tgcctgggcc ctcacccagc ctccctcaca gtctcctggc 600  
 cctcagtctc tccctccac tccatcctcc atctggcctc agtgggtcat tctgatcact 660  
 gaactgacca taccagccc tgcccacggc cctccatggc tcccaatgc cctggagagg 720  
 ggacatctag tcagagagta gtccctgaaga ggtggcctct gcgatgtgcc tgtgggggca 780  
 gcatcctgca gatggtccc gccctcatcc tctgacctg tctgcaggga ctgtcctcct 840  
 ggaccttgcc ccttgtgcag gagctggacc ctgaagtccc ctcccatag gccaaagactg 900  
 gagccttggt ccctctgttg gactccctgc ccatattctt gtgggagtg gttctggaga 960

```

catttctgtc tgttcctgag agctgggaat tgctctcagt catctgcctg cgcggttctg 1020
agagatggag ttgcctaggc agttattggg gccaatcttt ctactgtgt ctctcctcct 1080
ttaccttag ggtgattctg ggggtccact tgtctgtaat ggtgtgcttc aaggtatcac 1140
atcatggggc cctgagccat gtgcctgcc tgaaaagcct gctgtgtaca ccaaggtggt 1200
gcattaccgg aagtggatca aggacaccat cgcagccaac ccctgagtgc ccctgtccca 1260
cccctacctc tagtaaatTT aagtccacct cacgttctgg catcacttgg cctttctgga 1320
tgctggacac ctgaagcttg gaactcacct ggccgaagct cgagcctcct gagtccact 1380
gacctgtgct ttctggtgtg gagtccaggg ctgctaggaa aaggaatggg cagacacagg 1440
tgtatgccaa tgtttctgaa atgggtataa tttcgtcctc tccttcggaa cactggctgt 1500
ctctgaagac ttctcgtca gtttcagtga ggacacacac aaagacgtgg gtgacatgt 1560
tgtttgggg gtgcagagat gggaggggtg gggcccaccc tggagagtg gacagtga 1620
caaggtggac actctctaca gatcactgag gataagctgg agccacaatg catgaggcac 1680
acacacagca aggttgacgc tgtaaacata gccacgctg tcctgggggc actgggaagc 1740
ctagataagg ccgtgagcag aaagaagggg aggatcctcc tatgttgttg aaggagggac 1800
tagggggaga aactgaaagc tgattaatta caggagggtt gttcaggtcc cccaaaccac 1860
cgtcagattt gatgatttcc tagcaggact tacagaaata aagagctatc atgctgtggt 1920
ttattatggt ttgttacatt gataggatac atactgaaat cagcaaaca aacagatgta 1980
tagattagag tgtggagaaa acagaggaaa acttgcagtt acgaagactg gcaacttggc 2040
tttactaagt tttcagactg gcagggaagtc aaacctatta ggctgaggac cttgtggagt 2100
gtagctgac cagctgatag aggaactagc caggtggggg cctttccctt tggatggggg 2160
gcatatccga cagtatttct ctccaagtgg agacttacgg acagcatata attctccctg 2220
caaggatgta tgataatatg tacaagtaa ttccaactga ggaagctcac ctgatcctta 2280
gtgtccaagg ttttactgg ggtctgtag gacgagtatg gactacttga ataattgacc 2340
tgaagtcctc agacctgagg ttccctagag ttcaaacaga tacagcatgg tccagagtcc 2400
cagatgtaca aaaacaggga ttcatcaca atcccatctt tagcatgaag ggtctggcat 2460
ggcccaaggc cccaagtata tcaaggcact tgggcagaac atgccaaagg atcaaagtgc 2520
atctcccagg agttattcaa ggtgagccc tttacttggg atgtacaggc tttgagcagt 2580
gcaggtcctg tgagtcaacc tttattgta caggggatga gggaaaggga gaggatgagg 2640
aagccccctt ggggatttgg tttggtcttg tgatcaggtg gtctatgggg ctatccctac 2700
aaagaagaat ccagaaatag gggcacattg aggaatgata ctgagcccaa agagcattca 2760
atcattgttt tatttgcctt cttttcacac cattgggtgag ggagggatta ccaccctggg 2820
gttatgaaga tggttgaaca cccacacat agcaccggag atatgagatc aacagtttct 2880
tagccataga gattcacagc ccagagcagg aggcgctgc acaccatgca ggatgacatg 2940
ggggatgcgc tcgggatttg tgtgaagaag caaggactgt tagaggcagg ctttatagta 3000
acaagacggt ggggcaaact ctgatttccg tgggggaatg tcatggctct gctttactaa 3060
gttttgagac tggcaggtag tgaaactcat taggctgaga accttgtgga atgcagctga 3120
cccagctgat agaggaagta gccaggtggg agcctttccc agtgggtgtg ggacatatct 3180
ggcaagattt tgtggcactc ctggttacag atactggggc agcaataaaa actgaatctt 3240
gttttcagac cttaaaaaaa aaaaaaaa aaaagtttt 3279

```

&lt;210&gt; 383

&lt;211&gt; 155

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 383

```

Met Ala Gly Val Arg Asp Glu Gly Gln Gly Ala Arg Trp Pro His Thr
      5                                10                                15

```

```

Gly Lys Arg Gly Pro Leu Leu Gln Gly Leu Thr Trp Ala Thr Gly Gly
      20                                25                                30

```

```

His Cys Phe Ser Ser Glu Glu Ser Gly Ala Val Asp Gly Ala Gly Gln
      35                                40                                45

```

```

Lys Lys Asp Arg Ala Trp Leu Arg Cys Pro Glu Ala Val Ala Gly Phe
      50                                55                                60

```

```

Pro Leu Gly Ser Asp Cys Arg Glu Gly Gly Arg Gln Gly Cys Gly Gly
      65                                70                                75                                80

```

```

Ser Asp Asp Glu Asp Asp Leu Gly Val Ala Pro Gly Leu Ala Pro Ala

```

125

	85		90		95										
Trp	Ala	Leu	Thr	Gln	Pro	Pro	Ser	Gln	Ser	Pro	Gly	Pro	Gln	Ser	Leu
	100						105						110		
Pro	Ser	Thr	Pro	Ser	Ser	Ile	Trp	Pro	Gln	Trp	Val	Ile	Leu	Ile	Thr
	115						120					125			
Glu	Leu	Thr	Ile	Pro	Ser	Pro	Ala	His	Gly	Pro	Pro	Trp	Leu	Pro	Asn
	130					135					140				
Ala	Leu	Glu	Arg	Gly	His	Leu	Val	Arg	Glu						
	145					150									

<210> 384  
 <211> 557  
 <212> DNA  
 <213> Homo sapiens

<400> 384  
 ggatcctcta gagcgccgc ctactactac taaattcgcg gccgcgtcga cgaagaagag 60  
 aaagatgtgt tttgttttgg actctctgtg gtcccttcca atgctgtggg tttccaacca 120  
 ggggaagggt cccttttgca ttgccaagt ccataacat gagcactact ctaccatggg 180  
 tctgcctcct ggccaagcag gctggtttgc aagaatgaaa tgaatgattc tacagctagg 240  
 acttaacctt gaaatggaaa gtcttgcaat cccatttgca ggatccgtct gtgcacatgc 300  
 ctctgtagag agcagcattc ccagggacct tggaaacagt tggcactgta aggtgcttgc 360  
 tccccaagac acatcctaaa aggtgttgta atgggtgaaa cgtcttcctt ctttattgcc 420  
 ccttcttatt tatgtgaaca actggttgc tttttttgta tcttttttaa actgtaaagt 480  
 tcaattgtga aaatgaatat catgcaaata aattatgcga ttttttttc aaagtaaaaa 540  
 aaaaaaaaa aaaaaaa 557

<210> 385  
 <211> 337  
 <212> DNA  
 <213> Homo sapiens

<400> 385  
 ttcccagggt atgtgcgagg gaagacacat ttactatcct tgatggggct gattccttta 60  
 gtttctctag cagcagatgg gttaggagga agtgacccaa gtggttgact cctatgtgca 120  
 tctcaaagcc atctgctgtc ttcgagtacg gacacatcat cactcctgca ttgttgatca 180  
 aaacgtggag gtgcttttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240  
 tatcagacag gtccagtttc cgcaccaaca cctgctggtt ccctgtcgtg gtctggatct 300  
 ctttgccac caattcccc ttttccacat cccggca 337

<210> 386  
 <211> 300  
 <212> DNA  
 <213> Homo sapiens

<400> 386  
 gggcccgcta ccggcccagg ccccgccctcg cgagtccctc tccccgggtg cctgcccgcga 60  
 gcccgctcgg cccagagggt gggcgcgagg ctgcctctac cggctggcgg ctgtaactca 120  
 gcgaccttgg cccgaaggct ctagcaagga cccaccgacc ccagccgcg cggcggcggc 180  
 gcggactttg cccggtgtgt gggcgcgagc ggactgcgtg tccgcggacg ggcagcgaag 240  
 atgttagcct tcgctgccag gaccgtggac cgatcccagg gctgtggtgt aacctcagcc 300

<210> 387  
 <211> 537  
 <212> DNA  
 <213> Homo sapiens

126

&lt;400&gt; 387

```

gggccgagtc gggcaccaag ggactctttg caggcttcct tcctcggatc atcaaggctg 60
ccccctcctg tgccatcatg atcagcacct atgagttcgg caaaagcttc ttccagaggc 120
tgaaccagga cgggcttctg ggcggctgaa aggggcaagg aggcaaggac cccgtctctc 180
ccacggatgg ggagagggca ggaggagacc cagccaagtg ccttttctc agcactgagg 240
gagggggctt gtttcccttc cctcccggcg acaagctcca gggcagggct gtccctctgg 300
gcggcccagc acttctcag acacaacttc ttctgctgc tccagtcgtg gggatcatca 360
cttaccacc ccccaagttc aagaccaaat cttccagctg ccccttcgt gtttccctgt 420
gtttgctgta gctgggcatg tctccaggaa ccaagaagcc ctccagcctg ttagtctcc 480
ctgacccttg ttaattcctt aagtctaaag atgatgaact tcaaaaaaaa aaaaaa 537

```

&lt;210&gt; 388

&lt;211&gt; 520

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 388

```

aggataatTT ttaaaccaat caaatgaaaa aaacaaacaa acaaaaaagg aaatgtcatg 60
tgaggTTaaa ccagtttgca ttcccctaag gtggaaaaag taagaggact actcagcact 120
gtttgaagat tgcctctct acagcttctg agaattgtgt tatttcaact gccaaagtga 180
ggaccccttc cccaacatgc ccagcccac ccctaagcat ggtcccttgt caccaggcaa 240
ccaggaaact gctacttggt gacctacca gagaccagga gggtttggtt agctcacagg 300
acttccccca cccagaaga ttagcatccc atactagact cataactcaac tcaactaggc 360
tcataactcaa ttgatggTTa ttagacaatt ccatttcttt ctggttatta taaacagaaa 420
atctttcttc ttctcattac cagtaaaggc tcttggtatc tttctgttgg aatgatttct 480
atgaacttgt cttattttaa tgggtgggtt ttttctgtgt 520

```

&lt;210&gt; 389

&lt;211&gt; 365

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 389

```

cgttgcccc gtttgacaga aggaaaggcg gagcttattc aaagtctaga gggagtggag 60
gagTTaaagg tggatttcag atctgctgg ttccagccgc agtgtgccct ctgctcccc 120
aacgactttc caaataatct caccagcgcc ttccagctca ggcgtcctag aagcgtcttg 180
aagcctatgg ccagctgtct ttgtgtccc tctcaccgc ctgtcctcac agctgagact 240
cccaggaaac cttcagacta ccttctctg ccttcagcaa ggggcgttgc ccacattctc 300
tgagggtcag tggagaagcc tagactccca ttgctagagg tagaaagggg aagggtgctg 360
gggag

```

&lt;210&gt; 390

&lt;211&gt; 221

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(221)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 390

```

tgcctctcca tcctggcccc gacttctctg tcaggaaagt ggggatggac cccatctgca 60
tacacggnTT ctcattgggtg tggaaacatct ctgcttgctg ttccaggaag gcctctggct 120
gctctangag tctgancnga ntcgttgccc cantntgaca naaggaaagg cgagacttat 180
tcaaagtcta gagggagtgg aggagttaag gctggatttc a 221

```

&lt;210&gt; 391

&lt;211&gt; 325

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

127

<220>  
 <221> misc\_feature  
 <222> (1)...(325)  
 <223> n = A,T,C or G

<400> 391  
 tggagcaggt cccgaggcct ccctagagcc tggggccgac tctgtgncga tgcangcttt 60  
 ctctcgcgcc cagcctggag ctgctcctgg catctaccaa caatcagncg aggcgagcag 120  
 tagccagggc actgctgcca acagccagtc cmnataccat catgtnaccc ggtgngctct 180  
 naantngat ntccanagcc ctacccaten tagttctgct ctcccaccgg ntaccagccc 240  
 cactgcccag gaatcctaca gccagtaccc tgtcccgacg tctctaccta ccagtacgat 300  
 gagacctccg gctactacta tgacc 325

<210> 392  
 <211> 277  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(277)  
 <223> n = A,T,C or G

<400> 392  
 atattgttta actccttctt ttatatcttt taacattttc atggngaaaag gttcacatct 60  
 agtctcactt nggcagngn ctctacttg agtctcttcc ccggcctggn ccagtnngaa 120  
 antaccanga accgncatgn cttanaaacn ncctgggttn tgggttnntc aatgactgca 180  
 tgcagtgcac caccctgtcc actacgtgat gctgtaggat taaagtctca cagtgggcgg 240  
 ctgaggatac agcgccgcgt cctgtgttgc tggggaa 277

<210> 393  
 <211> 566  
 <212> DNA  
 <213> Homo sapiens

<400> 393  
 actagtcag tgtgttgga ttcgcggccg cgtcgacgga caggtcagct gtctggctca 60  
 gtgatctaca ttctgaagtt gtctgaaaat gtcttcatga ttaaattcag cctaaacggt 120  
 ttgccgggaa cactgcagag acaatgctgt gagtttccaa ccttagccca tctgcccggca 180  
 gagaaggctc agtttgtcca tcagcattat catgatatca ggactgggta ctgtgttaag 240  
 gaggggtcta ggagatctgt cccttttaga gacaccttac ttataatgaa gtatttggga 300  
 ggggtggttt caaaagtaga aatgtcctgt attccgatga tcatcctgta aacattttat 360  
 catttattaa tcatccctgc ctgtgtctat tattatattc atatctctac gctggaaaact 420  
 ttctgcctca atgtttactg tgcctttgtt tttgctagtt tgtgttgttg aaaaaaaaaa 480  
 cattctctgc ctgagtttta atttttgtcc aaagttattt taatctatac aattaaaagc 540  
 ttttgcctat caaaaaaaaa aaaaaa 566

<210> 394  
 <211> 384  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(384)  
 <223> n = A,T,C or G

<400> 394  
 gaacatacat gtcccggcac ctgagctgca gtctgacatc atcgccatca cgggcctcgc 60  
 tgcaaatng gaccgggcca aggcctggact gctggagcgt gtgaaggagc tacaggccna 120  
 gcaggaggac cgggctttta ggagttttta gctgagtgct actgtagacc ccaaatacca 180  
 tcccaagatt atcgggagaa agggggcagt aattacccaa atccgggttg agcatgacgt 240

gaacatccag tttcctgata aggacgatgg gaaccagccc caggaccaaa ttaccatcac 300  
 aggggtacgaa aagaacacag aagctgccag ggatgctata ctgagaattg tgggtgaact 360  
 tgagcagatg gtttctgagg acgt 384

<210> 395  
 <211> 399  
 <212> DNA  
 <213> Homo sapiens

<400> 395  
 ggcaaaactg tgtgacctca ataagacctc gcagatccaa ggtcaagtat cagaagtgc 60  
 tctgaccttg gactccaaga cctacatcaa cagcctggct atattagatg atgagccagt 120  
 tatcagaggt ttcattcattg cggaaattgt ggagtctaa gaaatcatgg cctctgaagt 180  
 attcagctct ttcaggtacc ctgagttctc tatagagttg cctaacacag gcagaattgg 240  
 ccagctactt gtctgcaatt gtatcttcaa gaataccctg gccatccctt tgactgacgt 300  
 caagttctct ttggaaagcc tgggcatctc ctactacag acctctgacc atgggacggt 360  
 gcagcctggt gagaccatcc aatcccaaat aaaatgcac 399

<210> 396  
 <211> 403  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(403)  
 <223> n = A,T,C or G

<400> 396  
 tggagtntc agtgcaaaca agccataaag cttcagtagc aaattactgt ctcacagaaa 60  
 gacattttca acttctgctc cagctgctga taaaacaaat catgtgttta gcttgactcc 120  
 agacaaggac aacctgttcc ttcataactc tctagagaaa aaaaggagtt gttagtagat 180  
 actaaaaaaa gtggatgaat aatctggata tttttcctaa aaagattcct tgaaacacat 240  
 taggaaaatg gagggcctta tgatcagaat gctagaatta gtccattgtg ctgaagcagg 300  
 gtttagggga gggagtggag gataaaagaa ggaaaaaag aagagtgaga aaacctattt 360  
 atcaaagcag gtgctatcac tcaatgttag gcctgctct ttt 403

<210> 397  
 <211> 100  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(100)  
 <223> n = A,T,C or G

<400> 397  
 actagtncag tgtggtggaa ttcgcggccg cgctcgaccta naanccatct ctatagcaaa 60  
 tccatccccg ctccctggtg gtnacagaat gactgacaaa 100

<210> 398  
 <211> 278  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(278)  
 <223> n = A,T,C or G

<400> 398

129

```

gcggccgcgt cgacagcagt tccgccagcg ctcgcccctg ggtgggggatg tgctgcacgc 60
ccacctggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120
tcactactgt gcctcgacca gtgaggagag ctggaccgac agcgagggtg actcatcatg 180
ctccgggcag cccatccacc tgtggcagtt cctcaaggag ttgctactca agccccacag 240
ctatggccgc ttcattangt ggctcaacaa ggagaagg 278

```

<210> 399  
 <211> 298  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(298)  
 <223> n = A,T,C or G

```

<400> 399
acggagggtgg aggaagcgnc cctgggatcg anaggatggg tcctgncatt gaccncctcn 60
ggggtgccng catggagcgc atgggcgcgg gcctgggcca cggcatggat cgcgtgggct 120
ccgagatcga gcgcatgggc ctggatcatgg accgcatggg ctccgtggag cgcgtgggct 180
ccggcattga gcgcatgggc ccgctgggccc tcgaccacat ggccctccanc attgancgca 240
tgggccagac catggagcgc attggctctg gcgtggagcn catgggtgcc ggcatggg 298

```

<210> 400  
 <211> 548  
 <212> DNA  
 <213> Homo sapiens

```

<400> 400
acatcaacta cttcctcatt ttaaggtatg gcagttccct tcatcccctt ttctgcctt 60
gtacatgtac atgtatgaaa ttctctctc ttaccgaact ctctccacac atcacaagggt 120
caaagaacca cacgcttaga agggtaaagag ggcaccctat gaaatgaaat ggtgatttct 180
tgagtctctt ttttccacgt ttaaggggcc atggcaggac ttagagttgc gagttaagac 240
tgacagagggc tagagaatta tttcatacag gctttgaggc caccatgtc acttatcccg 300
tataccctct caccatcccc ttgtctactc tgatgcccc aagatgcaac tgggcagcta 360
gttgccccca taattctggg cctttgttgt ttgttttaat tacttgggca tcccaggaag 420
ctttccagtg atctcctacc atgggcccc ctcctgggat caagcccctc ccaggccctg 480
tccccagccc ctctgcccc agcccacccg cttgccttgg tgctcagccc tcccattggg 540
agcaggtt 548

```

<210> 401  
 <211> 355  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(355)  
 <223> n = A,T,C or G

```

<400> 401
actgtttcca tggtatgttt ctacacattg ctacctcagt gtccttgga acttagcttt 60
tgatgtctcc aagtagtcca ccttcattta actctttgaa actgtatcat ctttgccaag 120
taagagtggg ggcctatttc agctgctttg acaaaaatgac tggctcctga cttaacgttc 180
tataaatgaa tgtgctgaag caaagtccc atggtggcgg cgaagaagan aaagatgtgt 240
tttgttttgg actctctgtg gtcccttcca atgctgnggg tttccaacca ggggaagggt 300
cccttttgca ttgccaagtg ccataaccat gagcactact ctaccatggn tctgc 355

```

<210> 402  
 <211> 407  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(407)  
 <223> n = A,T,C or G

<400> 402  
 atggggcaag ctggataaag aaccaagacc cactggagta tgctgtcttc aagaaaccca 60  
 tctcacatgc ggtggcatac ataggctcaa aataaaggaa tggagaaaaa tatttcaagc 120  
 aaatggaaaa cagaaaaaag caggtgttgc actcctactt tctgacaaaa cagactatgc 180  
 gaataaagat aaaaaagaga aggacattac aaagggtggtc ctgacctttg ataatctca 240  
 ttgcttgata ccaacctggg ctgttttaat tgcccaaacc aaaaggataa tttgctgagg 300  
 ttgtggagct tctcccctgc agagagtccc tgatctccca aaatttggtt gagatgtaag 360  
 gntgattttg ctgacaactc cttttctgaa gttttactca tttccaa 407

<210> 403  
 <211> 303  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(303)  
 <223> n = A,T,C or G

<400> 403  
 cagtatttat agccnaactg aaaagctagt agcaggcaag tctcaaatcc aggcacccaaa 60  
 tcctaagcaa gagccatggc atggtgaaaa tgcaaaagga gagtctggcc aatctacaaa 120  
 tagagaacaa gacctactca gtcatgaaca aaaaggcaga caccaacatg gatctcatgg 180  
 gggattggat attgtaatta tagagcagga agatgacagt gatcgtcatt tggcacaca 240  
 tcttaacaac gaccgaaacc cattattttac ataaacctcc attcggtaac catgttgaaa 300  
 gga 303

<210> 404  
 <211> 225  
 <212> DNA  
 <213> Homo sapiens

<400> 404  
 aagtgtaaact tttaaaaatt tagtggattt tgaaaattct tagaggaaag taaaggaaaa 60  
 attgttaatg cactcattta cttttacatg gtgaaagtgc tctcttgatc ctacaaacag 120  
 acattttcca ctctgtgttc catagtgtgt aagtgtatca gatgtgttgg gcatgtgaat 180  
 ctccaagtgc ctgtgtaata aataaagtat ctttatttca ttcat 225

<210> 405  
 <211> 334  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(334)  
 <223> n = A,T,C or G

<400> 405  
 gagctgttat actgtgagtt ctactaggaa atcatcaaat ctgagggttg tctggaggac 60  
 ttcaatacac ctccccccat agtgaatcag cttccagggg gtccagtcce tctccttact 120  
 tcacccccat cccatgccaa aggaagaccc tccctccttg gctcacagcc ttctctagge 180  
 ttcccagtgc ctccaggaca gagtgggtta tgttttcagc tccatccttg ctgtgagtgt 240  
 ctggtgcggt tgtgcctcca gcttctgctc agtgcctcat ggacagtgtc cagcccatgt 300  
 cactctccac tctctcanng tggatccac ccct 334



<210> 406  
 <211> 216  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(216)  
 <223> n = A,T,C or G

<400> 406  
 tttcatacct aatgagggag ttganatnac atnnaaccag gaaatgcatg gatctcaang 60  
 gaaacaaaca cccaataaac tcggagtggc agactgacaa ctgtgagaca tgcacttgct 120  
 acnaaacaca aatttnatgt tgcacccttg tttctacacc tgtgggttat gacaaagaca 180  
 actgccaaag aatnttcaag aaggaggact gccant 216

<210> 407  
 <211> 413  
 <212> DNA  
 <213> Homo sapiens

<400> 407  
 gctgacttgc tagtâtcatc tgcattcatt gaagcacaag aacttcacgc cttgactcat 60  
 gtaaatgcaa taggattaaa aaataaattt gatatacat ggaaacagac aaaaaatatt 120  
 gtacaacatt gcacccagtgc tcagattcta cacctggcca ctgaggaagc aagagttaat 180  
 cccagagggtc tatgtcctaa tgtgttatgg caaatggatg tcatgcacgt accttcattt 240  
 ggaaaattgt catttgtcca tgtgacagtt gatacttatt cacatttcat atgggcaacc 300  
 tgccagacag gagaaagtct tcccatgtta aaagacattt attatcttgt tttcctgtca 360  
 tgggagttcc agaaaaagtt aaaacagaca atgggccagg ttctgtagta aag 413

<210> 408  
 <211> 183  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(183)  
 <223> n = A,T,C or G

<400> 408  
 ggagctngcc ctcaattcct ccatntctat gttancatat ttaatgtctt ttgnnattaa 60  
 tnccttaacta gttaatcctt aaagggtan ntaatcctta actagtcctt ccattgtgag 120  
 cattatcctt ccagtattcn ccttctnttt tatttactcc ttcttggtta cccatgtact 180  
 ntt 183

<210> 409  
 <211> 250  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(250)  
 <223> n = A,T,C or G

<400> 409  
 cccacgcatg ataagctctt tatttctgta agtcctgcta ggaaatcatc aaatctgacg 60  
 gtggtttggg ggacctgaac aaacctcctg taattaatca gctttcagtt tctcccccta 120  
 gtccctcctt caacaacata ggaggatcct ccccttcttt ctgtcacagg ccttatctag 180  
 gcttcccagt gcccccagga cagcgtgggc tatgtttaca gcgcntcctt gctggggggg 240  
 ggccntatgc 250

<210> 410  
<211> 306  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(306)  
<223> n = A,T,C or G

<400> 410  
ggctggtttg caagaatgaa atgaatgatt ctacagctag gacttaacct tgaaatggaa 60  
agtcttgcaa tcccatattgc aggatccgctc tgtgcacatg cctctgtaga gaggcagcatt 120  
cccaggagacc ttggaaacag ttggcactgt aagggtgcttg ctccccaaga cacatcctaa 180  
aagggtgttg aatggtgaaa accgcttctt tctttattgc cccttcttat ttatgtgaac 240  
nactggttgg ctttttttgn atctttttta aactggaaag ttcaattgng aaaatgaata 300  
tcntgc 306

<210> 411  
<211> 261  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(261)  
<223> n = A,T,C or G

<400> 411  
agagatattn cttaggtnaa agttcataga gttcccatga actatatgac tggccacaca 60  
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120  
tttaaattgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180  
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttaccat cagttccagc 240  
cttctctcaa gngaggcaa a 261

<210> 412  
<211> 241  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(241)  
<223> n = A,T,C or G

<400> 412  
gttcaatggt acctgacatt tctacaacac cccactcacc gatgtattcg ttgccagtg 60  
ggaacatacc agcctgaatt tggaaaaaat aattgtgttt cttgccagc aaatactacg 120  
actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggaggggag 180  
ctgggagatt tactgggta cattgaattc ccaaactacc cangcaatta ccagccaac 240  
a 241

<210> 413  
<211> 231  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(231)  
<223> n = A,T,C or G

<400> 413  
aactcttaca atccaagtga ctcatctgtg tgcttgaatc ctttccactg tctcatctcc 60  
ctcatccaag ttcttagtac cttctctttg ttgtgaagga taatcaaact gaacaacaaa 120  
aagttttact tcctcatttg gaacctaaaa actctcttct tcctgggtct gagggctcca 180  
agaatccttg aatcanttct cagatcattg gggacaccan atcaggaacc t 231

<210> 414  
<211> 234  
<212> DNA  
<213> Homo sapiens

<400> 414  
actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60  
gatggagctg aaaacataac ccactctgtc ctggaggcac tgggaagcct agagaaggct 120  
gtgagccaag gagggagggt cttccttttg catgggatgg ggatgaagta aggagaggga 180  
ctggaccccc tgggaagctga ttcactatgg ggggagggtg attgaagtcc tcca 234

<210> 415  
<211> 217  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(217)  
<223> n = A,T,C or G

<400> 415  
gcataggatt aagactgagt atcttttcta cattctttta acttttctaag gggcacttct 60  
caaaacacag accaggtagc aaatctccac tgctctaagg ntctcaccac cacttttctca 120  
cacctagcaa tagtagaatt cagtcctact tctgaggcca gaagaatggt tcagaaaaat 180  
antggattat aaaaaataac aattaagaaa aataatc 217

<210> 416  
<211> 213  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(213)  
<223> n = A,T,C or G

<400> 416  
atgcatatnt aaagganact gcctcgcttt tagaagacat ctggnctgct ctctgcatga 60  
ggcacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120  
cgaatgcaag gtgggttaatt gaaggccact aattgatgct caaatagaag gatattgact 180  
atattggaac agatggagtc tctactacaa aag 213

<210> 417  
<211> 303  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(303)  
<223> n = A,T,C or G

<400> 417  
nagtcttcag gccatcagg gaagttcaca ctggagagaa gtcatacata tgtactgtat 60

134

```

gtgggaaagg ctttactctg agttcaaata ttcaagccca tcagagagtc cacactggag 120
agaagccata caaatgcaat gagtgtggga agagcttcag gagggattcc cattatcaag 180
ttcatctagt ggtccacaca ggagagaaac cctataaatg tgagatatgt gggaagggct 240
tcantcaaag ttcgtatctt caaatccatc ngaaggncca cagtatanan aaacctttta 300
agt 303

```

```

<210> 418
<211> 328
<212> DNA
<213> Homo sapiens

```

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<220>
<221> misc_feature
<222> (1)...(328)
<223> n = A,T,C or G

```

```

<400> 418
tttttgccgg tgggtgggca gggacgggac angagtctca ctctgttgcc caggctggag 60
tgcacaggca tgatctcggc tcaactacaac ccctgcctcc catgtccaag cgattcttgt 120
gcctcagcct tccctgtagc tagaattaca ggacacatgcc accacaccca gctagttttt 180
gtatttttag tagagacagg gtttcacccat gttggccagg ctggtctcaa actcctnacc 240
tcagnggtca ggctggtctc aaactcctga cctcaagtga tctgcccacc tcagcctccc 300
aaagtgctan gattacaggc cgtgagcc 328

```

```

<210> 419
<211> 389
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> (1)...(389)
<223> n = A,T,C or G

```

```

<400> 419
cctcctcaag acggcctgtg gtcgcctccc cggcaaccaa gaagcctgca gtgccatag 60
acccctgagc catggactgg agcctgaaag gcagcgtaca ccctgctcct gatcttgctg 120
cttgtttctt ctctgtggct ccattcatag cacagtgtgt gcaactgaggc ttgtgcaggc 180
cgagcaaggc caagctggct caaagagcaa ccagtcaact ctgccacggg gtgccaggca 240
ccggttctcc agccaccaac ctcaactcgt cccgcaaagt gcacatcagt tcttctaccc 300
taaaggtagg accaaagggc atctgctttt ctgaagtccct ctgctctatc agccatcacg 360
tggcagccac tcnggctgtg tcgacgcgg 389

```

```

<210> 420
<211> 408
<212> DNA
<213> Homo sapiens

```

```

<400> 420
gttcctccta actcctgcca gaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gctttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggg gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg aagtgcctatg acaaacctgg caagcccg 408

```

```

<210> 421
<211> 352
<212> DNA
<213> Homo sapiens

```

<220>  
 <221> misc\_feature  
 <222> (1)...(352)  
 <223> n = A,T,C or G

<400> 421  
 gctcaaaaat ctttttactg atnggcatgg ctacacaatc attgactatt acggaggcca 60  
 gaggagaatg aggcctggcc tgggagccct gtgcctacta naagcacatt agattatcca 120  
 ttcactgaca gaacaggctt tttttgggtc cttcttctcc accacnatac acttgcagtc 180  
 ctcttcttgg aagattcttt ggcaagtgtc tttgtcataa cccacagggt tagaaacaag 240  
 ggtgcaacat gaaatttctg tttcgtagca agtgcattgc tcacaagttg gcangtctgc 300  
 cactccgagt ttattgggtg tttgtttcct ttgagatcca tgcatttcct gg 352

<210> 422  
 <211> 337  
 <212> DNA  
 <213> Homo sapiens

<400> 422  
 atgccaccat gctggcaatg cagcggggcg tcgaaggcct gcatatccag cccaagctgg 60  
 cgatgatcga cggcaaccgt tgcccgaagt tgccgatgcc agccgaagcg gtggtcaagg 120  
 gcgatagcaa ggtgccggcg atcgcgcgcg cgtcaatcct ggccaaggtc agccgtgac 180  
 gtgaaatggc agctgtcgaa ttgatctacc cgggttatgg catcggcggg cataagggtc 240  
 atccgacacc ggtgcacctg gaagccttgc agcggctggg gccgacgccc attcaccgac 300  
 gcttcttccg ccggtacggc tggcctatga aaattat 337

<210> 423  
 <211> 310  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(310)  
 <223> n = A,T,C or G

<400> 423  
 gctcaaaaat ctttttactg atatggcatg gctacacaat cattgactat tagaggccag 60  
 aggagaatga ggcctggcct gggagccctg tgccactan aagcncatta gattatccat 120  
 tcaactgacag aacaggcttt ttttgggtcc ttcttctcca ccacgatata cttgcagtc 180  
 tccttcttga agattctttg gcagttgtct ttgtcataac ccacagggtg anaaacaagg 240  
 gtgcaacatg aaatttctgt ttcgtagcaa gtgcattgtc cacagttgtc aagtctgcc 300  
 tccgagttta 310

<210> 424  
 <211> 370  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(370)  
 <223> n = A,T,C or G

<400> 424  
 gctcaaaaat ctttttactg ataggcatgg ctacacaatc attgactatt agaggccaga 60  
 ggagaatgag gcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120  
 cactgacaga acaggctttt tttgggtcct tcttctccac cagcatatac ttgcagtcct 180  
 ccttcttgaa gattctttgg cagttgtctt tgtcataacc cacagggtga gaaacatcct 240  
 ggttgaatct cctggaactc cctcattagg tatgaaatag catgatgcat tgcataaagt 300  
 cacgaagggt gcaaagatca caacgctgcc cagganaaca ttcattgtga taagcaggac 360  
 tccgtcgacg 370

136

<210> 425  
 <211> 216  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(216)  
 <223> n = A,T,C or G

<400> 425  
 aattgctatn ntttattttg ccactcaaaa taattaccaa aaaaaaaaaa tnttaaata 60  
 taacaacnca acatcaaggn aaananaaca ggaatggntg actntgcata aatnggccga 120  
 anattatcca ttatnttaag gggtgacttc aggtacagc acacagacaa acatgcccg 180  
 gaggtnttca ggaccgctcg atgtntttng aggagg 216

<210> 426  
 <211> 596  
 <212> DNA  
 <213> Homo sapiens

<400> 426  
 cttccagtga ggataaccct gttgccccgg gccgagggtc tccattaggc tctgattgat 60  
 tggcagtcag tgatggaagg gtgttctgat cattccgact gccccaaggg tgcgtggcca 120  
 gctctctgtt ttgctgagtt ggcagtagga cctaatttgt taattaagag tagatggtga 180  
 gctgtccttg tattttgatt aacctaatgg ccttcccagc acgactcgga ttcagctgga 240  
 gacatcacgg caacttttaa tgaaatgatt tgaagggccca ttaagaggca cttcccgta 300  
 ttaggcagtt catctgcact gataacttct tggcagctga gctggtcgga gctgtggccc 360  
 aaacgcacac ttggcttttg gttttgagat acaactctta atcttttagt catgcttgag 420  
 ggtggatggc cttttcagct ttaacccaat ttgcaactgc ttggaagtgt agccaggaga 480  
 atacactcat atactcgtgg gcttagaggc cacagcagat gtcattggtc tactgcctga 540  
 gtcccgtggtg tcccatccca ggaccttcca tcggcgagta cctgggagcc cgtgct 596

<210> 427  
 <211> 107  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(107)  
 <223> n = A,T,C or G

<400> 427  
 gaagaattca agttaggttt attcaaaggg cttacngaga atcctanacc caggncccg 60  
 cccgggagca gccttanaga gtcctgttt gactgcccgg ctcagn 107

<210> 428  
 <211> 38  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(38)  
 <223> n = A,T,C or G

<400> 428  
 gaacttcna anaangactt tattcactat tttacatt 38

<210> 429

<211> 544  
<212> DNA  
<213> Homo sapiens

<400> 429  
ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60  
attgaagagc ggctgcagcc ctgcgggttca gattaaaatc cgagaattgt atagacgccg 120  
atatccacga actcttgaag gactttctga tttatccaca atcaaatacat cggttttcag 180  
tttgatggt ggctcatcac ctgtagaacc tgacttgcc gtggctggaa tccactcgtt 240  
gccttccact tcagttacac ctcaactcacc atcctctcct gttggttctg tgcgtcttca 300  
agataactaag cccacatttg agatgcagca gccatctccc ccaattcctc ctgtccatcc 360  
tgatgtgcag ttaaaaaatc tgccttttta tgatgtcctt gatgttctca tcaagccac 420  
gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttattt ttgctttgac 480  
acctcaaca gtttagagaga tatgcatatc cagggatttt ttgccagggt gtaggagaga 540  
ttat 544

<210> 430  
<211> 507  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(507)  
<223> n = A,T,C or G

<400> 430  
cttatcncaa tggggctccc aaacttggt gtgcagtga aactccgggg gaattttgaa 60  
gaacactgac acccatcttc caccgccgaca ctctgattta attgggtgc agtgagaaca 120  
gagcatcaat ttaaaaagct gcccagaatg ttntcctggg cagcgttggt atctttgccn 180  
ccttcgtgac tttatgcaat gcatcatgct atttcatacc taatgaggga gttccaggag 240  
attcaaccag gatgtttcta cncctgtggg ttatgacaaa gacaactgcc aaagaatntt 300  
caagaaggag gactgcaagt atatcgtggt ggagaagaag gacccaaaaa agacctgttc 360  
tgtcagtga tggataatct aatgtgcttc tagtaggcac agggctccca ggccaggcct 420  
cattctctc tggcctctaa tagtcaatga ttgtgtagcc atgcctatca gtaaaaagat 480  
ttttgagcaa aaaaaaaaaa aaaaaaa 507

<210> 431  
<211> 392  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(392)  
<223> n = A,T,C or G

<400> 431  
gaaaattcag aatggataaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60  
aaacaagaaa gcacttatca ggaggactta caaatggaag tacactctan aaccatcatc 120  
tatcatggct aaatgtgaga ttagcacagc tgtattattt gtacattgca aacacctaga 180  
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtcctgggtt ttccaacaga 240  
catcattcca gcattctgag attagggnga ttgggatca ttctggaggt ggaatgttca 300  
acaaaagtga tgttgttagg taaaatgtac aacttctgga tctatgcaga cattgaaggt 360  
gcaatgagtc tggcttttac tctgctgttt ct 392

<210> 432  
<211> 387  
<212> DNA  
<213> Homo sapiens

<220>

138

<221> misc\_feature  
 <222> (1)...(387)  
 <223> n = A,T,C or G

<400> 432  
 ggtatccnta cataatcaaa tatagctgta gtacatgttt tcattggngt agattaccac 60  
 aaatgcaagg caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg 120  
 ngtagtccaa gctctcggna gtccagccac tngaaaacat gctcccttta gattaacctc 180  
 gtggacnctn ttgttgnatt gtctgaactg tagngccctg tatttttgctt ctgtctgnga 240  
 attctgttgc ttctggggca ttcccttgng atgcagagga ccaccacaca gatgacagca 300  
 atctgaattg ntccaatcac agctgcgatt aagacatact gaaatcgtac aggaaccggga 360  
 acaacgtata gaacactgga gtccttt 387

<210> 433  
 <211> 281  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(281)  
 <223> n = A,T,C or G

<400> 433  
 ttcaactagc anagaanact gcttcagggg gtgtaaaatg aaaggcttcc acgcagttat 60  
 ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120  
 caggcnctat ttgggttggc tggaggagct gtggaaaaca tggagagatt ggcgctggag 180  
 atcgccgtgg ctattcctcn ttgntattac accagngagg ntctctgtnt gccactgggt 240  
 tnnaaaaccg ntatacaata atgatagaat aggacacaca t 281

<210> 434  
 <211> 484  
 <212> DNA  
 <213> Homo sapiens

<400> 434  
 ttttaaaata agcatttagt gctcagtcoc tactgagtag tctttctctc ccctcctctg 60  
 aatttaattc tttcaacttg caatttgcaa ggattacaca ttctactgtg atgtatattg 120  
 tggtgcaaaa aaaaaaaagt gtctttgttt aaaattactt ggtttgtgaa tccatcttgc 180  
 tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240  
 agctagtcta tcagcatctg acagggtgaat tggatgggtc tcagaacccat ttcacccaga 300  
 cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca taacaaaccc 360  
 tgctccaatc tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420  
 tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag taccatgtc 480  
 tttta 484

<210> 435  
 <211> 424  
 <212> DNA  
 <213> Homo sapiens

<400> 435  
 gcgcgctca gagcaggtca ctttctgcct tccacgtcct ccttcaagga agcccatgt 60  
 gggtagcttt caatatcgca ggttcttact cctctgcctc tataagctca aaccaccaa 120  
 cgatcgggca agtaaacccc ctccctcgcc gacttcggaa ctggcgagag ttcagcgag 180  
 atgggcctgt ggggaggggg caagatagat gagggggagc ggcatgggtc ggggtgaccc 240  
 cttggagaga ggaaaaaggc cacaagaggg gctgccaccg ccaactaacg agatggccct 300  
 ggtagagacc tttgggggtc tggaacctct ggactcccca tgctctaact cccacactct 360  
 gctatcagaa acttaaaactt gaggattttc tctgtttttc actcgcaata aattcagagc 420  
 aaac 424

<210> 436



<211> 667  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(667)  
<223> n = A,T,C or G

<400> 436  
accttgggaa nactctcaca atataaaggg tcgtagactt tactccaaat tccaaaaagg 60  
tcctggccat gtaatcctga aagttttccc aaggtagcta taaaatcctt ataaggggtgc 120  
agcctcttct ggaattcctc tgatttcaaa gtctcactct caagttcttg aaaacgaggg 180  
cagttcctga aaggcaggta tagcaactga tcttcagaaa gaggaactgt gtgcaccggg 240  
atgggctgcc agagttagat aggattccag atgctgacac cttctggggg aaacaggggt 300  
gccaggtttg tcatagcact catcaaagtc cggccaacgt ctgtgcttcg aatataaacc 360  
tgttcagtgt tataggactc attcaagaat tttctatata tctttcttat atactctcca 420  
agttcataat gctgctccat gccagctgg gtgagttggc caaatccttg tggccatgag 480  
gattccttta tgggtcagtg gggaaagggt tcaatgggac ttcggtctcc atgccgaaac 540  
accaaagtca caaacttcaa cctctgggt agtacacttc ggtctagcca gaaaaaagc 600  
agaaacaaga agccaaggct aaggcttgct gccctgccag gaggaggggt gcagctctca 660  
tgttgag 667

<210> 437  
<211> 693  
<212> DNA  
<213> Homo sapiens

<400> 437  
ctacgtctca accctcattt ttaggtaagg aatcttaagt ccaaagatat taagtgactc 60  
acacagccag gtaaggaaag ctggattggc aactaggac tctaccatac cgggttttgt 120  
taaagctcag gttaggaggc tgataagctt ggaaggaaact tcagacagct ttttcagatc 180  
ataaaagata attcttagcc catgttcttc tccagagcag acctgaaatg acagcacagc 240  
aggtaactct ctattttcac cctcttgct tctactctct ggcagtcaga cctgtgggag 300  
gccatgggag aaagcagctc tctggatgtt tgtacagatc atggactatt ctctgtggac 360  
catttctcca ggttacccta ggtgtcacta ttggggggac agccagcatc tttagctttc 420  
atttgagttt ctgtctgtct tcagtagagg aaacttttgc tctcacact tcacatctga 480  
acacctaact gctgttgctc ctgaggtggg gaaagacaga tatagagctt acagtattta 540  
tcctatttct aggcactgag ggctgtgggg tacctgtgg tgccaaaaca gatcctggtt 600  
taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgttg gctctttacc 660  
ctgcatcatg tgctctcttg gctgaaaatg acc 693

<210> 438  
<211> 360  
<212> DNA  
<213> Homo sapiens

<400> 438  
ctgcttatca caatgaatgt tctcctgggc agcgttggtga tctttgccac ettcgtgact 60  
ttatgcaatg catcatgcta tttcatacct aatgagggag ttccaggaga ttcaaccagg 120  
atgtttctac acctgtgggt tatgacaaag acaactgcc aagaatcttc aagaaggagg 180  
actgcaagta tatctgtggg agaagaagga cccaaaaaag acctgttctg tcagtgaatg 240  
gataatctaa tgtgcttcta gtaggcacag ggctcccagg ccaggcctca ttctcctctg 300  
gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360

<210> 439  
<211> 431  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature

&lt;222&gt; (1)...(431)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 439

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gttcctnnta actcctgcc a gaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttcc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtccata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
aatttagtag t                                     431

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&lt;210&gt; 440

&lt;211&gt; 523

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 440

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agagataaag cttaggtcaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg ttttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaccca atttaccat cagttccagc 240
cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300
actgaaaaac tgctactatc tgtttttata tttctgttaa aatatatgag gctacagaac 360
taaaaattaa aacctctttg tgtcccttgg tcctggaaca tttatgttcc ttttaaagaa 420
acaaaaatca aactttacag aaagatttga tgtatgtaac acatatagca gctcttgaag 480
tatatatatc atagcaaata agtcatctga tgagaacaag cta                                     523

```

&lt;210&gt; 441

&lt;211&gt; 430

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 441

```

gttcctccta actcctgcc a gaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttcc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtccata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
aatttagtag                                     430

```

&lt;210&gt; 442

&lt;211&gt; 362

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 442

```

ctaaggaatt agtagtgttc ccatcacttg tttggagtgt gctattctaa aagattttga 60
tttcctggaa tgacaattat attttaactt tgggtgggga aagagttata ggaccacagt 120
cttcacttct gatacttgta aattaactt ttattgcact tgttttgacc attaaagctat 180
atgttttagaa atggtcattt tacggaaaaa ttagaaaaat tctgataata gtgcagaata 240
aatgaattaa tgttttactt aatttatatt gaactgtcaa tgacaaataa aaattctttt 300
tgattatttt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360
tc                                     362

```

&lt;210&gt; 443

&lt;211&gt; 624

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

141

<220>  
<221> misc\_feature  
<222> (1)...(624)  
<223> n = A,T,C or G

<400> 443  
ttttttttt gcaacacaat atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60  
ttgaaagaat taaattcaga ggaggggaga gaaagagtag tcagtaggga ctgagcacta 120  
aatgcttatt ttaaaagaaa tgtaaagagc agaaagcaat tcaggctacc ctgccttttg 180  
tgctggctag tactccggtc ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240  
cccaaaccac agaaaatggg gtgaaattgg ccaactttct attaacttgg cttcctgttt 300  
tataaaatat tgtgaataat atcacctact tcaaagggca gttatgaggc ttaaatgaac 360  
taacgcctac aaaacactta aacatagata acataggtgc aagtactatg tatctggtac 420  
atggtaaaca tccttattat taaagtcaac gctaaaatga atgtgtgtgc atatgcta 480  
agtacagaga gagggcactt aaaccaacta agggcctgga gggaaggttt cctggaaaga 540  
ngatgcttgt gctgggtcca aatcttggtc tactatgacc ttggccaaat tatttaaact 600  
ttgtccctat ctgctaaaca gatc 624

<210> 444  
<211> 425  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(425)  
<223> n = A,T,C or G

<400> 444  
gcacatcatt nntcttgcatt tctttgagaa taagaagatc agtaaatagt tcagaagtgg 60  
gaagctttgt ccaggcctgt gtgtgaaccc aatgttttgc ttagaaatag aacaagtaag 120  
ttcattgcta tagcataaca caaaatttgc ataagtgggt gtcagcaaat ccttgaatgc 180  
tgcttaatgt gagaggttgg taaaatcctt tgtgcaacac tctaactccc tgaatgtttt 240  
gctgtgctgg gacctgtgca tgccagacaa ggccaagctg gctgaaagag caaccagcca 300  
cctctgcaat ctgccacctc ctgctggcag gatttgtttt tgcacacctg gaagagccaa 360  
ggaggcacca gggcataagt gagtagactt atggtcgacg cggccgcgaa tttagtagta 420  
gtaga 425

<210> 445  
<211> 414  
<212> DNA  
<213> Homo sapiens

<220>  
<221> misc\_feature  
<222> (1)...(414)  
<223> n = A,T,C or G

<400> 445  
catgtttatg nttttggatt actttgggca cctagtgttt ctaaactcgtc tatcattctt 60  
ttctgttttt caaaagcaga gatggccaga gtctcaacaa actgtatctt caagtctttg 120  
tgaaattctt tgcatgtggc agattattgg atgtagtctt ctttaactag catataaatc 180  
tggtgtgttt cagataaatg aacagcaaaa tgtgggtgaa ttaccatttg gaacattgtg 240  
aatgaaaaat tgtgtctcta gattatgtaa caaataacta tttcctaacc attgatcttt 300  
ggatttttat aatcctactc acaaatgact aggtctctcc tcttgtattt tgaagcagt 360  
tgggtgctgg attgataaaa aaaaaaaaaa tcgacgcggc gcggaattta gtag 414

<210> 446  
<211> 631  
<212> DNA  
<213> Homo sapiens

142

<220>  
 <221> misc\_feature  
 <222> (1)...(631)  
 <223> n = A,T,C or G

<400> 446  
 acaaattaga anaaagtgcc agagaacacc acataccttg tccggaacat tacaatggct 60  
 tctgcatgca tgggaagtgt gagcattcta tcaatatgca ggagccatct tgcagggtgtg 120  
 atgctggtta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttggtc 180  
 ccggtcctgt acgatttcag tatgtcttaa tcgcagctgt gattggaaca attcagattg 240  
 ctgtcatctg tgtggtggtc ctctgcatca caagggccaa actttaggta atagcattgg 300  
 actgagattt gtaaaacttc caaccttcca ggaaatgcc cagaagcaac agaattcaca 360  
 gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420  
 taatctaaag ggagcatggt tcacagtggc tggactaccg agagcttgga ctacacaata 480  
 cagtattata gacaaaagaa taagacaaga gatctacaca tgttgccctg catttggtgtg 540  
 aatctacacc aatgaaaaca tgtactacag ctatatattga ttatgtatgg atatatttga 600  
 aatagtatac attgtcttga tgtttttct g 631

<210> 447  
 <211> 585  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(585)  
 <223> n = A,T,C or G

<400> 447  
 ccttgggaaa antntcacia tataaagggc cgtagacttt actccaaatt ccaaaaaggt 60  
 cctggccatg taatcctgaa agttttccca aggtagctat aaaatcctta taaggggtgca 120  
 gcctcttctg gaattcctct gatttcaaag tctcactctc aagttcttga aaacgagggc 180  
 agttcctgaa aggcaggtat agcaactgat cttcagaaaag aggaactgtg tgcaccggga 240  
 tgggctgcca gagtaggata ggattccaga tgcgtacacc ttctggggga aacagggctg 300  
 ccaggtttgt catagcactc atcaaagtcg ggtcaacgtc tgtgcttcga atataaacct 360  
 gttcatgttt ataggactca ttcaagaatt ttctatatct ctttcttata tactctccaa 420  
 gttcataatg ctgctccatg cccagctggg tgagttggcc aaatccttgt ggccatgagg 480  
 attcctttat ggggtcagtg ggaaaggtgt caatggggact tcggtctcca tgccgaaaca 540  
 ccaaagtcac aaacttcaac tccttggtta gtacacttcg gtcta 585

<210> 448  
 <211> 93  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(93)  
 <223> n = A,T,C or G

<400> 448  
 tgctcgtggg tcattctgan nccgaactg accntgccag ccctgccgan gggccnccat 60  
 ggctccctag tgccctggag agganggggc tag 93

<210> 449  
 <211> 706  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature

&lt;222&gt; (1)...(706)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 449

```

ccaagttcat gctntgtgct ggacgctgga caggggggcaa aagcnnttgc tcgtgggtca 60
ttctgancac cgaactgacc atgccagccc tgccgatggt cctccatggc tccctagtgc 120
cctggagagg aggtgtctag tcagagagta gtcctggaag gtggcctctg ngaggagcca 180
cggggacagc atcctgcaga tggtcgggcg cgtcccatc gccattcagg ctgcgcaact 240
gttgggaagg gcgatcggtg cgggcctctt cgctattacg ccagctggcg aaagggggat 300
gtgctgcaag gcgattaaat tgggtaacgc cagggtttcc ccagtcncga cgttgtaaaa 360
cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcattgcacg 420
cgtacgtaag cttggatcct ctagagcggc cgcctactac tactaaattc gcggccgcgt 480
cgacgtggga tcncactga gagagtggag agtgacatgt gctggacnct gtccatgaag 540
cactgagcag aagctggagg cacaacgcnc cagacactca cagctactca ggaggctgag 600
aacaggttga acctgggagg tggagggtgc aatgagctga gatcaggccn ctgcncacca 660
gcatggatga cagagtgaaa ctccatctta aaaaaaaaaa aaaaaa 706

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&lt;210&gt; 450

&lt;211&gt; 493

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 450

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gagacggagt gtcactctgt tgcccaggct ggagtgcagc aagacactgt ctaagaaaaa 60
acagttttta aaggtaaaac aacataaaaa gaaatatcct atagtggaaa taagagagtc 120
aaatgaggct gagaacttta caaagggatc ttacagacat gtcgccaata tcaactgcatg 180
agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ggtacaattc 240
caagtcagggt agtgaatgg gtggaattaa actcaaatta atcctgccag ctgaaacgca 300
agagacactg tcagagagtt aaaaagttag ttctatccat gaggtgattc cacagtcttc 360
tcaagtcacac acatctgtga actcacagac caagttctta aaccactgtt caaactctgc 420
tacacatcag aatcacctgg agagctttac aaactcccat tgccgagggt cgacgcggcc 480
gcgaatttag tag 493

```

&lt;210&gt; 451

&lt;211&gt; 501

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(501)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 451

```

gggcgcgtcc cattcgccat tcaggctgcg caactgttgg gaagggcgat cgggtcgggc 60
ctcttcgcta ttacgccagc tggcgaaaag gggatgtgct gcaaggcgat taagttgggt 120
aacgccaggg ttttcccagt cncgacgttg taaaacgacg gccagtgaat tgaatttagg 180
tgacnctata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atcctctaga 240
gcggccgcct actactacta aattcgcggc cgcgtcgacg tgggatccnc actgagagag 300
tgagagtgta catgtgctgg acnctgtcca tgaagcactg agcagaagct ggagggcaca 360
cgcncacagc actcacagct actcaggagg ctgagaacag gttgaacctg ggaggtggag 420
gttgcaatga gctgagatca ggccnctgcn cccagcatg gatgacagag tgaaactcca 480
tcttaaaaaa aaaaaaaaaa a 501

```

&lt;210&gt; 452

&lt;211&gt; 51

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(51)

144

&lt;223&gt; n = A,T,C or G

<400> 452  
 agacggtttc accnttaciaa cnccttttag gatgggnntt ggggagcaag c 51

<210> 453  
 <211> 317  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)...(317)  
 <223> n = A,T,C or G

<400> 453  
 tacatcttgc tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa 60  
 acatctgaag agctagtcta tcagcatctg gcaagtgaat tggatgggtc tcagaaccat 120  
 ttcacccana cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca 180  
 taacaaaccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240  
 cccaccaaac tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300  
 taccatgtc tttatta 317

<210> 454  
 <211> 231  
 <212> DNA  
 <213> Homo sapiens

<400> 454  
 ttcgaggta aatcaactct cagagtgtag tttccttcta tagatgagtc agcattaata 60  
 taagccacgc cagcctcttg aaggagtctt gaattctcct ctgctcactc agtagaacca 120  
 agaagaccaa attcttctgc atcccagctt gcaaacaaaa ttgttcttct aggtctccac 180  
 ccttctttt tcagtgttcc aaagctcctc acaatttcat gaacaacagc t 231

<210> 455  
 <211> 231  
 <212> DNA  
 <213> Homo sapiens

<400> 455  
 taccaaagag ggcataataa tcagtctcac agtaggggtc accatcctcc aagtgaaaaa 60  
 cattgttccg aatgggcttt ccacaggcta cacacacaaa acaggaaaca tgccaagttt 120  
 gtttcaacgc attgatgact tctccaagga tcttcctttg gcacgcacca cattcagggg 180  
 caaagaattt ctcatagcac agctcacaat acagggctcc tttctcctct a 231

<210> 456  
 <211> 231  
 <212> DNA  
 <213> Homo sapiens

<400> 456  
 ttggcaggta cccttacaaa gaagacacca taccttatgc gttattaggt ggaataatca 60  
 ttccattcag tattatcggtt attattcttg gagaaaccct gtctgtttac tgtaaccttt 120  
 tgcactcaaa ttcctttatc aggaataact acatagccac tatttataaa gccattggaa 180  
 cctttttatt tgggtgcagct gctagtcagt ccctgactga cattgccaag t 231

<210> 457  
 <211> 231  
 <212> DNA  
 <213> Homo sapiens

&lt;220&gt;

145

<221> misc\_feature  
<222> (1)...(231)  
<223> n = A,T,C or G

<400> 457  
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tatttgattt tattagcaat ctctttcaga agacccttga gatcattaag ctttgtatcc 180  
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<213> Homo sapiens

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<213> Homo sapiens

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<213> Homo sapiens

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<210> 461  
<211> 231  
<212> DNA  
<213> Homo sapiens

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<213> Homo sapiens

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146

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<212> DNA  
<213> Homo sapiens

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<210> 464  
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<212> DNA  
<213> Homo sapiens

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cctgtctcag tgactgtgtg cctgtagtcc cagctactcg ggagtctgtg tgaggccagg 180  
ggtgccacgc caccagctag atgctctgta acttctaggc ccattttcc c 231

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<212> DNA  
<213> Homo sapiens

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<212> DNA  
<213> Homo sapiens

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 468

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&lt;210&gt; 469

&lt;211&gt; 2229

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 469

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aatggaatt

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&lt;210&gt; 470

&lt;211&gt; 2426

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 470

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&lt;210&gt; 471

&lt;211&gt; 812

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 471

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&lt;210&gt; 472

&lt;211&gt; 515

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; misc\_feature

&lt;222&gt; (1)...(515)

&lt;223&gt; n = A,T,C or G

&lt;400&gt; 472

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150

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gaaaaaaaaa naaaaaaaaa aaanaaaan aaaaa 515

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&lt;210&gt; 473

&lt;211&gt; 750

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 473

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Arg Pro Arg Trp Leu Cys Ala Gly Ala Leu Val Leu Ala Gly Gly Phe
      20              25              30

Phe Leu Leu Gly Phe Leu Phe Gly Trp Phe Ile Lys Ser Ser Asn Glu
      35              40              45

Ala Thr Asn Ile Thr Pro Lys His Asn Met Lys Ala Phe Leu Asp Glu
      50              55              60

Leu Lys Ala Glu Asn Ile Lys Lys Phe Leu Tyr Asn Phe Thr Gln Ile
      65              70              75              80

Pro His Leu Ala Gly Thr Glu Gln Asn Phe Gln Leu Ala Lys Gln Ile
      85              90              95

Gln Ser Gln Trp Lys Glu Phe Gly Leu Asp Ser Val Glu Leu Ala His
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Tyr Asp Val Leu Leu Ser Tyr Pro Asn Lys Thr His Pro Asn Tyr Ile
      115             120             125

Ser Ile Ile Asn Glu Asp Gly Asn Glu Ile Phe Asn Thr Ser Leu Phe
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Glu Pro Pro Pro Pro Gly Tyr Glu Asn Val Ser Asp Ile Val Pro Pro
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Phe Ser Ala Phe Ser Pro Gln Gly Met Pro Glu Gly Asp Leu Val Tyr
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Val Asn Tyr Ala Arg Thr Glu Asp Phe Phe Lys Leu Glu Arg Asp Met
      180             185             190

Lys Ile Asn Cys Ser Gly Lys Ile Val Ile Ala Arg Tyr Gly Lys Val
      195             200             205

Phe Arg Gly Asn Lys Val Lys Asn Ala Gln Leu Ala Gly Ala Lys Gly
      210             215             220

Val Ile Leu Tyr Ser Asp Pro Ala Asp Tyr Phe Ala Pro Gly Val Lys
      225             230             235             240

Ser Tyr Pro Asp Gly Trp Asn Leu Pro Gly Gly Gly Val Gln Arg Gly
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Asn Ile Leu Asn Leu Asn Gly Ala Gly Asp Pro Leu Thr Pro Gly Tyr

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Leu Pro Phe Asp Cys Arg Asp Tyr Ala Val Val Leu Arg Lys Tyr Ala  
 595 600 605  
 Asp Lys Ile Tyr Ser Ile Ser Met Lys His Pro Gln Glu Met Lys Thr  
 610 615 620  
 Tyr Ser Val Ser Phe Asp Ser Leu Phe Ser Ala Val Lys Asn Phe Thr  
 625 630 635 640  
 Glu Ile Ala Ser Lys Phe Ser Glu Arg Leu Gln Asp Phe Asp Lys Ser  
 645 650 655  
 Asn Pro Ile Val Leu Arg Met Met Asn Asp Gln Leu Met Phe Leu Glu  
 660 665 670  
 Arg Ala Phe Ile Asp Pro Leu Gly Leu Pro Asp Arg Pro Phe Tyr Arg  
 675 680 685  
 His Val Ile Tyr Ala Pro Ser Ser His Asn Lys Tyr Ala Gly Glu Ser  
 690 695 700  
 Phe Pro Gly Ile Tyr Asp Ala Leu Phe Asp Ile Glu Ser Lys Val Asp  
 705 710 715 720  
 Pro Ser Lys Ala Trp Gly Glu Val Lys Arg Gln Ile Tyr Val Ala Ala  
 725 730 735  
 Phe Thr Val Gln Ala Ala Ala Glu Thr Leu Ser Glu Val Ala  
 740 745 750

&lt;210&gt; 474

&lt;211&gt; 386

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 474

Met Arg Ala Ala Pro Leu Leu Leu Ala Arg Ala Ala Ser Leu Ser Leu  
 5 10 15  
 Gly Phe Leu Phe Leu Leu Phe Phe Trp Leu Asp Arg Ser Val Leu Ala  
 20 25 30  
 Lys Glu Leu Lys Phe Val Thr Leu Val Phe Arg His Gly Asp Arg Ser  
 35 40 45  
 Pro Ile Asp Thr Phe Pro Thr Asp Pro Ile Lys Glu Ser Ser Trp Pro  
 50 55 60  
 Gln Gly Phe Gly Gln Leu Thr Gln Leu Gly Met Glu Gln His Tyr Glu  
 65 70 75 80  
 Leu Gly Glu Tyr Ile Arg Lys Arg Tyr Arg Lys Phe Leu Asn Glu Ser  
 85 90 95  
 Tyr Lys His Glu Gln Val Tyr Ile Arg Ser Thr Asp Val Asp Arg Thr  
 100 105 110  
 Leu Met Ser Ala Met Thr Asn Leu Ala Ala Leu Phe Pro Pro Glu Gly  
 115 120 125  
 Val Ser Ile Trp Asn Pro Ile Leu Leu Trp Gln Pro Ile Pro Val His

130	135	140
Thr Val Pro Leu Ser Glu Asp Gln Leu Leu Tyr Leu Pro Phe Arg Asn 145 150 155 160		
Cys Pro Arg Phe Gln Glu Leu Glu Ser Glu Thr Leu Lys Ser Glu Glu 165 170 175		
Phe Gln Lys Arg Leu His Pro Tyr Lys Asp Phe Ile Ala Thr Leu Gly 180 185 190		
Lys Leu Ser Gly Leu His Gly Gln Asp Leu Phe Gly Ile Trp Ser Lys 195 200 205		
Val Tyr Asp Pro Leu Tyr Cys Glu Ser Val His Asn Phe Thr Leu Pro 210 215 220		
Ser Trp Ala Thr Glu Asp Thr Met Thr Lys Leu Arg Glu Leu Ser Glu 225 230 235 240		
Leu Ser Leu Leu Ser Leu Tyr Gly Ile His Lys Gln Lys Glu Lys Ser 245 250 255		
Arg Leu Gln Gly Gly Val Leu Val Asn Glu Ile Leu Asn His Met Lys 260 265 270		
Arg Ala Thr Gln Ile Pro Ser Tyr Lys Lys Leu Ile Met Tyr Ser Ala 275 280 285		
His Asp Thr Thr Val Ser Gly Leu Gln Met Ala Leu Asp Val Tyr Asn 290 295 300		
Gly Leu Leu Pro Pro Tyr Ala Ser Cys His Leu Thr Glu Leu Tyr Phe 305 310 315 320		
Glu Lys Gly Glu Tyr Phe Val Glu Met Tyr Tyr Arg Asn Glu Thr Gln 325 330 335		
His Glu Pro Tyr Pro Leu Met Leu Pro Gly Cys Ser Pro Ser Cys Pro 340 345 350		
Leu Glu Arg Phe Ala Glu Leu Val Gly Pro Val Ile Pro Gln Asp Trp 355 360 365		
Ser Thr Glu Cys Met Thr Thr Asn Ser His Gln Gly Thr Glu Asp Ser 370 375 380		
Thr Asp 385		
<210> 475		
<211> 261		
<212> PRT		
<213> Homo sapiens		
<400> 475		
Met Trp Val Pro Val Val Phe Leu Thr Leu Ser Val Thr Trp Ile Gly 5 10 15		
Ala Ala Pro Leu Ile Leu Ser Arg Ile Val Gly Gly Trp Glu Cys Glu 20 25 30		

Lys	His	Ser	Gln	Pro	Trp	Gln	Val	Leu	Val	Ala	Ser	Arg	Gly	Arg	Ala
35						40			45						
Val	Cys	Gly	Gly	Val	Leu	Val	His	Pro	Gln	Trp	Val	Leu	Thr	Ala	Ala
50						55				60					
His	Cys	Ile	Arg	Asn	Lys	Ser	Val	Ile	Leu	Leu	Gly	Arg	His	Ser	Leu
65				70						75				80	
Phe	His	Pro	Glu	Asp	Thr	Gly	Gln	Val	Phe	Gln	Val	Ser	His	Ser	Phe
				85				90						95	
Pro	His	Pro	Leu	Tyr	Asp	Met	Ser	Leu	Leu	Lys	Asn	Arg	Phe	Leu	Arg
		100						105				110			
Pro	Gly	Asp	Asp	Ser	Ser	His	Asp	Leu	Met	Leu	Leu	Arg	Leu	Ser	Glu
		115				120						125			
Pro	Ala	Glu	Leu	Thr	Asp	Ala	Val	Lys	Val	Met	Asp	Leu	Pro	Thr	Gln
130						135				140					
Glu	Pro	Ala	Leu	Gly	Thr	Thr	Cys	Tyr	Ala	Ser	Gly	Trp	Gly	Ser	Ile
145				150						155				160	
Glu	Pro	Glu	Glu	Phe	Leu	Thr	Pro	Lys	Lys	Leu	Gln	Cys	Val	Asp	Leu
				165				170						175	
His	Val	Ile	Ser	Asn	Asp	Val	Cys	Ala	Gln	Val	His	Pro	Gln	Lys	Val
		180						185				190			
Thr	Lys	Phe	Met	Leu	Cys	Ala	Gly	Arg	Trp	Thr	Gly	Gly	Lys	Ser	Thr
		195				200						205			
Cys	Ser	Gly	Asp	Ser	Gly	Gly	Pro	Leu	Val	Cys	Asn	Gly	Val	Leu	Gln
210						215				220					
Gly	Ile	Thr	Ser	Trp	Gly	Ser	Glu	Pro	Cys	Ala	Leu	Pro	Glu	Arg	Pro
225				230						235				240	
Ser	Leu	Tyr	Thr	Lys	Val	Val	His	Tyr	Arg	Lys	Trp	Ile	Lys	Asp	Thr
				245				250						255	
Ile	Val	Ala	Asn	Pro											
		260													

<210> 476

**<211> 1079**

&lt;212&gt; PRT

<213> Homo sapiens

<400> 476

Met His His His His His His Met Trp Val Pro Val Val Phe Leu Thr  
5 10 15

Leu Ser Val Thr Trp Ile Gly Ala Ala Pro Leu Ile Leu Ser Arg Ile  
20 25 30

Val Gly Gly Trp Glu Cys Glu Lys His Ser Gln Pro Trp Gln Val Leu  
35 40 45



Val Ala Ser Arg Gly Arg Ala Val Cys Gly Gly Val Leu Val His Pro  
 50 55 60  
 Gln Trp Val Leu Thr Ala Ala His Cys Ile Arg Asn Lys Ser Val Ile  
 65 70 75 80  
 Leu Leu Gly Arg His Ser Leu Phe His Pro Glu Asp Thr Gly Gln Val  
 85 90 95  
 Phe Gln Val Ser His Ser Phe Pro His Pro Leu Tyr Asp Met Ser Leu  
 100 105 110  
 Leu Lys Asn Arg Phe Leu Arg Pro Gly Asp Asp Ser Ser His Asp Leu  
 115 120 125  
 Met Leu Leu Arg Leu Ser Glu Pro Ala Glu Leu Thr Asp Ala Val Lys  
 130 135 140  
 Val Met Asp Leu Pro Thr Gln Glu Pro Ala Leu Gly Thr Thr Cys Tyr  
 145 150 155 160  
 Ala Ser Gly Trp Gly Ser Ile Glu Pro Glu Glu Phe Leu Thr Pro Lys  
 165 170 175  
 Lys Leu Gln Cys Val Asp Leu His Val Ile Ser Asn Asp Val Cys Ala  
 180 185 190  
 Gln Val His Pro Gln Lys Val Thr Lys Phe Met Leu Cys Ala Gly Arg  
 195 200 205  
 Trp Thr Gly Gly Lys Ser Thr Cys Ser Gly Asp Ser Gly Gly Pro Leu  
 210 215 220  
 Val Cys Asn Gly Val Leu Gln Gly Ile Thr Ser Trp Gly Ser Glu Pro  
 225 230 235 240  
 Cys Ala Leu Pro Glu Arg Pro Ser Leu Tyr Thr Lys Val Val His Tyr  
 245 250 255  
 Arg Lys Trp Ile Lys Asp Thr Ile Val Ala Asn Pro Gly Ser Met Ala  
 260 265 270  
 Thr Ala Gly Asn Pro Trp Gly Trp Phe Leu Gly Tyr Leu Ile Leu Gly  
 275 280 285  
 Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile Asn Gly  
 290 295 300  
 Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met  
 305 310 315 320  
 Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val  
 325 330 335  
 Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly  
 340 345 350  
 Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu  
 355 360 365  
 Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala  
 370 375 380

Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp  
 385 390 395 400  
 Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn  
 405 410 415  
 Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro  
 420' 425 430  
 Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys  
 435 440 445  
 Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly  
 450 455 460  
 Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro  
 465 470 475 480  
 Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala  
 485 490 495  
 Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys  
 500 505 510  
 Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser Glu Phe Met Val  
 515 520 525  
 Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala Gln Leu  
 530 535 540  
 Leu Leu Val Asn Leu Leu Thr Phe Gly Leu Glu Val Cys Leu Ala Ala  
 545 550 555 560  
 Gly Ile Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val Glu Glu  
 565 570 575  
 Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly Leu Val  
 580 585 590  
 Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly Arg Tyr  
 595 600 605  
 Gly Arg Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile Leu Leu  
 610 615 620  
 Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu Leu Cys  
 625 630 635 640  
 Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly Val Gly  
 645 650 655  
 Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu Ala Leu  
 660 665 670  
 Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala Tyr Ser  
 675 680 685  
 Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr Leu Leu  
 690 695 700  
 Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu Gly Thr

705		710		715		720
Gln Glu Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu Thr Cys						
		725		730		735
Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly Pro Thr						
		740		745		750
Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His Cys Cys						
		755		760		765
Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu Leu Pro						
		770		775		780
Arg Leu His Gln Leu Cys Cys Arg Met Pro Arg Thr Leu Arg Arg Leu						
		785		790		795
800						
Phe Val Ala Glu Leu Cys Ser Trp Met Ala Leu Met Thr Phe Thr Leu						
		805		810		815
Phe Tyr Thr Asp Phe Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg						
		820		825		830
Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg						
		835		840		845
Met Gly Ser Leu Gly Leu Phe Leu Gln Cys Ala Ile Ser Leu Val Phe						
		850		855		860
Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val						
		865		870		875
880						
Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys						
		885		890		895
Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu Thr Gly						
		900		905		910
Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala Ser Leu						
		915		920		925
Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly Asp Thr						
		930		935		940
Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu Pro Gly						
		945		950		955
960						
Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala Gly Gly						
		965		970		975
Ser Gly Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser Ala Cys						
		980		985		990
Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala Arg Val						
		995		1000		1005
Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp Ser Ala						
		1010		1015		1020
Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser Ile Val						
		1025		1030		1035
1040						

Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala Gly Leu  
1045 1050 1055

Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp Lys Ser  
1060 1065 1070

Asp Leu Ala Lys Tyr Ser Ala  
1075